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Examining Biobehavioral Variables and Predictors Associated with Pressure Injury Development in Cardiac Surgery Patients Undergoing Ventricular Assist Device and Total Artificial Heart Surgery.

A Dissertation Submitted in Partial Fulfillment of The Requirements for The Degree of Doctor of Philosophy at Virginia Commonwealth University.

By

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Abstract

BACKGROUND

Cardiac surgery patients have some of the highest reported incidence and prevalence of pressure injuries (PI). A growing subset of cardiac surgery include patients with end-stage heart failure who undergo ventricular assist device (VAD) or total artificial heart (TAH) surgery. The risk of PI and their natural history of development in this population are unknown and the specific risk factors for PI development remain unexplored.

OBJECTIVES

To perform a systematic review of the literature to identify the incidence and risk factors of PI development in patients undergoing VAD-TAH surgery and thereby inform study design and variables in an eight-year retrospective study of all patients undergoing VAD-TAH surgery at a large academic university medical center.

METHODS

The preferred reporting items for systematic reviews and meta-analyses or PRISMA statement guided this systematic review. Quality of evidence was determined using the Johns Hopkins Nursing Evidence-Based Practice Rating Scale. Two reviewers independently appraised manuscripts matching the eligibility criteria for study inclusion. Four databases including PubMed, CINAHL, Web of Science, Google Scholar, and hand searches of journals based on reference lists from included studies were utilized. Initial results of this primary search revealed zero studies that met inclusion and this search methodology was confirmed by medical librarian consultation. Therefore, a follow up retrospective study was necessary to identify incidence of PI in the VAD-TAH population. However, a secondary search, dropping keywords of VAD-TAH and instead focusing on studies of *on-pump* cardiac surgery and mixed surgical studies where cardiac surgery patients were included, was conducted to establish variables to guide a retrospective study of all VAD-TAH surgeries between 2010-2018. The retrospective study evaluated the incidence of pressure ulcers by case, patient and incidence density for each of the respective 1000 patient days during the study period. Univariate statistics are reported by four different VAD-TAH devices. Variables significant in bivariate analysis were entered in a stepwise logistic regression model.

RESULTS

In the systematic review, 312 articles were identified from the databases with eight additional articles from hand searches. Following abstract review, 208 were excluded for not meeting inclusion criteria or study quality metrics. 77 articles were read in full, with 61 excluded, leaving 16 articles for inclusion. 31 risk factors were identified for PI development in *on-pump* cardiac surgery patients with 11 risk factors which were identified as significant in multivariate analysis for inclusion in the retrospective study.

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The final sample for investigation in the retrospective study included 292 independent VAD-TAH surgical cases conducted in 265 patients. In total, 32 patients developed 45 PI. The incidence of PI per all surgical cases was 11% (32/292), with PI incidence per patient of 12% (32/265). Incidence density was found to be (10/1000) 1% for 2010-2012, (12/1000) 1.2% for 2013-2015, and (10/920) 1.1% for 2016-2018 respectively. Logistic regression analysis revealed the following significant predictor variables for pressure injury in the VAD-TAH population: age, mechanical ventilation time and preoperative Braden Risk Assessment score.

CONCLUSIONS

The overall incidence of PI was much lower than anticipated given historical incidence of PI in non-device cardiac surgery patients. This population may be at higher risk of PI development due to: greater severity of illness preoperatively, longer operating room times, longer cardiopulmonary bypass time, and associated comorbidities, among others. However, given the low incidence of PI found in this study compared to historical comparisons of Coronary Artery Bypass Graft patients, a prospective study to further investigate significant risk factors and identify potential preventive mechanisms that decreased PI incidence in this population is warranted.

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Manuscript #1

Incidence and Predictor Variables of Pressure Injuries in Patients Undergoing Ventricular Assist Device and Total Artificial Heart Surgeries: A Systematic Review.

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ABSTRACT

BACKGROUND

Cardiac surgery patients have some of the highest reported incidence and prevalence of pressure injuries (PI). A growing subset of cardiac surgery include patients with end-stage heart failure who undergo ventricular assist device (VAD) or total artificial heart (TAH) surgery. The risk of PI and their natural history of development in this population are unknown.

OBJECTIVES

To perform a systematic review of the literature to identify the prevalence, incidence, and risk factors of PI development in patients undergoing VAD-TAH surgery.

METHODS

The preferred reporting items for systematic reviews and meta-analyses or PRISMA statement guided this systematic review. Quality of evidence was determined using the Johns Hopkins Nursing Evidence-Based Practice Rating Scale. Two reviewers independently appraised manuscripts matching the eligibility criteria for study inclusion. Four databases including PubMed, CINAHL, Web of Science, Google Scholar, and hand searches of journals based on reference lists from included studies were utilized. Initial results of this primary search revealed zero studies that met inclusion and this search methodology was confirmed by medical librarian consultation. A secondary search dropping keywords of VAD-TAH and instead focusing on studies of *on-pump* cardiac surgery and mixed surgical studies where cardiac surgery patients were included was conducted.

RESULTS

312 articles were identified from the databases with eight additional articles from hand searches. Following abstract review, 208 were excluded for not meeting inclusion criteria or study quality metrics. 77 articles were read in full, with 61 excluded, leaving 16 articles for inclusion. 31 risk factors were identified for PI development in *on-pump* cardiac surgery patients with 11 risk factors being most commonly identified as significant in multivariate analysis across all studies.

CONCLUSIONS

The prevalence, incidence and natural history of PI in VAD-TAH patients remains unknown. This population may be at higher risk of PI development due to: greater severity of illness preoperatively, longer operating room times, longer cardiopulmonary bypass time, and associated comorbidities, among others. The results of risk factors associated with *on-pump* cardiac surgery patients will guide a subsequent 8-year retrospective study of the PI risk factors that potentially confront VAD-TAH patients, to gain more insight into PI development in this subset of the cardiac surgery population.

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INTRODUCTION

Pressure ulcers are defined as, "localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear" [1]. In 2016, the term pressure ulcer was revised to pressure injury by the National Pressure Ulcer Advisory Panel (NPUAP) and this term was defined as, "localized damage to the skin and underlying soft tissue usually over a bony prominence or related to a medical or other device. The injury occurs because of intense and/or prolonged pressure or pressure in combination with shear. The tolerance of soft tissue for pressure and shear may also be affected by microclimate, nutrition, perfusion, comorbid conditions and condition of the soft tissue"[2]. The revisions were made to attempt to more adequately reflect PI staging, particularly of Stage 1 and Deep Tissue Pressure Injury, as these pressure and shear related injuries do not always ulcerate.

Globally, PI prevalence ranges from 27.3% to 72.5%. [1,3]. In acute care settings, prevalence ranges from 0-49% contingent on the care setting and patient population. Over 2.5 million patients develop PI and cause 60,000 deaths in the United States per year [4]. In the U.S., PI treatment costs may exceed $26.8 billion dollars annually [5], increase length of stay (LOS) by 11 days, and adds $30,000 to overall costs per admission. [6–9] Over 100 risk factors have been associated with the development of PI. Historically, cardiac surgery patients have been described as at high risk for PI development with incidence rates between 7-29.5% [10–17]. Risk factors for identification of PI in cardiac surgery patients remains a needed and clinically relevant area of research given the high incidence, cost, associated patient burden and lack of advancement in prevention of PI in cardiac surgery patients [18,19].

Heart Failure and VAD-TAH Surgeries

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A growing subset of the cardiac surgery patient population includes those with advancing heart failure (HF) who require implantable ventricular assist devices or a total artificial heart (VAD-TAH). In the U.S., the number of persons with HF is anticipated to exceed eight million people by 2030 and is projected to be the leading cause of disability [20]. One retrospective study in patients hospitalized with systolic HF investigated LOS, in-hospital mortality and associated predictors. Data were extrapolated from three payer based research databases [21]. Of the 17,517 patients identified in the study, PI were present in 4% of subjects with associated increased LOS by 1.36 days ($p<0.0001$) due to PI in every payer category (commercial 158/4109; Medicaid 76/2118; Medicare 446/11,370), evidencing a significant patient and economic burden. The use of VAD-TAH devices is becoming the standard of care for both bridge-to-transplant and long-term destination therapy in end stage HF. Between 2009 and 2014, the percentage of heart transplant recipients who had a VAD at the time of transplant increased from 33.6% (n=631) to 44.9% (n=1018) [22]. In an interrupted time series intervention study of 341 patients in two cardiac surgery intensive care units, the only statistically significant variable for PI development was heart failure ($p=0.002$) [15]. Due to the high rate of PI in the cardiac surgery population, the impact of VAD-TAH surgery on PI development warrants investigation.

Patients undergoing VAD-TAH procedures may be at greater risk for PI development compared to patients requiring a Coronary Artery Bypass Graft (CABG) procedure related to: 1) nature and length of the VAD-TAH procedure including cardiopulmonary bypass, 2) length of stay (LOS), and 3) physiological vulnerability and comorbidities of patients with advanced HF. The VAD-TAH procedure has greater surgical times than CABG (3-6 hours for CABG vs. 6-9 hours VAD-TAH), plus higher total immobility, defined henceforth as the total time from preoperative admission in the perioperative suite to first turn in the intensive care unit post

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operatively. Average LOS for CABG surgery is five days, while VAD and TAH average LOS is 20 and 18 days, respectively (Cotts et al., 2014; [24]. Finally, patients who need VAD-TAH have advanced heart failure with severely reduced cardiac function, whereas patients who undergo CABG have coronary artery occlusion with or without existing heart failure. This differentiation is significant. Patients with advanced left ventricular failure or biventricular failure requiring VAD-TAH have higher preoperative American Society of Anesthesia (ASA) scale scores compared to patients having CABG. ASA scale scores range from I (mild systemic disease) to V (moribund patient not expected to survive without surgical intervention [25]. ASA scores greater than or equal to three are associated with higher operating room PI rates [26]. Fred and colleagues (2012) reported that for each one-point increase in ASA, the odds of developing PI increased by 149% in a sample of 138 surgical patient from mixed specialties in a retrospective review.

CARDIOPULMONARY BYPASS

Cardiopulmonary bypass (CPB) creates a non-pulsatile, bloodless surgical field while reintroducing oxygenated blood back into the systemic circulation [27]. Use of CPB is associated with multisystem organ dysfunction including cardiac, pulmonary, renal, hepatic, gastric and cerebral failure. The severity and extent of organ failure depends on the duration of: CPB, surgery, aortic cross clamping and plasma lactate levels [28]. A systematic review of 23 studies with a total sample size of 7,976 patients identified that on-pump cardiac surgery patients had significantly higher incidence of stroke, renal failure, ventilation time and sternal infection [29]. Systemic inflammation and subsequent organ and tissue damage is further complicated by the non-pulsatile nature of blood flow associated with CPB. Systemic changes associated with CPB include a severe systemic inflammatory response syndrome caused by activation of both cellular and solid proteins [27] as described in TABLE 1. Alterations to vascular permeability and tissue edema is most

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profound in patients undergoing CPB for 80 minutes or longer [30]. Despite the focus of much research on injury to body organs from CBP, the effect of CPB on the skin has not been reported.

Given the high prevalence of PI associated with CABG procedure and the additional vulnerability associated with advanced HF and VAD-TAH surgical procedures, it is hypothesized that the VAD-TAH surgery represents the highest level of risk for PI development among cardiac surgery patients. However, the actual incidence is unknown and represents a large gap in our current understanding of PI etiology in this population.

Therefore, the aim of this systematic review of the literature is to describe the prevalence, incidence and risk factors associated with PI development in heart failure patients undergoing ventricular assist device or total artificial heart (VAD-TAH) surgery.

METHODS

The design for systematic review of the literature utilized the methods described in the preferred reporting items for systematic reviews or PRISMA statement [35]. Strength and quality of evidence was determined using the Johns Hopkins Nursing Evidence-Based Practice Rating Scale seen in Figure 1 [36]. Risk of bias associated with the identified studies was determined using the Cochrane tool for assessing risk of bias [37].

Inclusion criteria for the systematic review involved studies reporting the development of PIs in cardiac surgery patients undergoing VAD or TAH surgery. Specifically, retrospective or prospective observational studies reporting study incidence or prevalence of pressure injuries within the perioperative, intraoperative or immediate postoperative period were considered. Study characteristics including English only language and a timeframe of 1966-2017 to coincide with the

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first reported implantation of a mechanical support device for myocardial recovery after heart surgery [38].

Informational sources utilized for study identification and inclusion included PubMed, CINAHL, Web of Science, Google Scholar, and hand searches of journals based on reference lists from included studies. Two search strings of keywords utilized for PubMed and CINAHL databases including associated filters are show in Figure 2. For these initial searches, 240 articles were found, 30 were selected after abstract review, however after full text review, 0 articles were identified that included VAD or TAH patients which reported on PI risk factors, incidence, prevalence or natural history within these patients. The results were validated by the inclusion of a medical librarian who confirmed via independent search the inability to identify any articles matching the eligibility criteria for this systematic review.

Secondary Review

Therefore, a secondary search was conducted *removing* keywords specific to ventricular assist device and total artificial heart and focusing on *on-pump* cardiac surgical procedures. The same databases were utilized. The search included a revision to the eligibility criteria which included only studies from 2007 to the present. This decision follows the changes to the National Pressure Ulcer Advisory Panel's updated pressure ulcer staging system [39] which included the addition of suspected deep tissue injury and unstageable pressure ulcer classifications. Further, the time frame is justified as the morbidity of cardiac surgical patients is considerably different in the last 10 years than during the historical period between 1966-2007. Further inclusion criteria allowed, 1) all retrospective or prospective studies including patients undergoing on-pump (e.g. use of cardiopulmonary bypass during cardiac surgery) cardiac surgery procedures or 2) reported systematic reviews and meta-analyses of cardiac surgery patients and 3) studies of intraoperative

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PI risk where cardiovascular surgery patients were part of the sample. Grey literature was evaluated and included if such sources described research studies with sufficient methodological description to determine strength of evidence and quality. Articles that were strength of evidence lower than III and/or quality scores of C or less were excluded. Similarly, articles were not included if designated as off-pump cardiac surgery or vascular/thoracic procedures. Duplicates and reprinted publications were removed to reduce the risk of transverse and longitudinal bias. A flow diagram of study records identified can be found in Figure 3. Search data and identified study records were managed with Excel spreadsheet software in chronological order with the authors (TB & JB) reviewing each full text article independently for inclusion, strength of evidence and quality, as well as risk of bias. Following review, these records were extrapolated to the evidence table shown in Table 1.

On-pump cardiac surgery with CPB cannot be compared to other non-cardiac surgeries due to the differences in perioperative, operative and postoperative patient characteristics [32]. Therefore, articles including off-pump cardiac surgery, or beating heart surgery, were removed secondary to the CPB research indicating that off-pump patients are at considerably less risk for complications including multisystem organ failure [33]. Since off-pump surgical technique was developed in the mid-1990s, it was assumed any articles that did not differentiate on-versus-off pump CABG were on-pump, given reports that the use of off-pump technique was negligible in 1995, about 10% in 1999 and estimated to be around 50% by 2005 [40].

RESULTS

ON-PUMP CARDIAC SURGERY STUDIES

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Based on the outcomes of the VAD-TAH review as described above, the secondary aim of this systematic review was to identify articles involving on-pump cardiac surgery patients that represent the closest surrogate for the VAD-TAH population. In total, 312 articles were identified from the respective databases with eight additional articles identified by hand searches. Following abstract review, 208 were excluded for not meeting the appropriate surgical type, procedure, date range or study quality metrics. Seventy-seven articles were reviewed, with 60 excluded secondary to: reprints, non-English language, being off-pump populations, vascular or thoracic procedures and poor strength of evidence and quality scores. An evidence table of all 17 included articles is provided in TABLE 2. Seven articles included studies involving cardiac surgery patients only, whereas nine included mixed surgical populations in addition to ICU and operating room locations. Common risk factors found between the respective studies who performed multivariate analysis are found in TABLE 3.

Cardiac Surgery Population

Feuchtinger and colleagues (2007) identified that 33/53 consecutively enrolled CABG patients developed 47% of ulcers on post-operative day 0 and 15% of the remaining pressure injuries between day 1 and day 7 after surgery. The primary limitation of this study was the high rate of attrition as patients were dropped from the study after they left the ICU. The primary purpose of this study was to compare post-operative risk assessment scores or predict PI development using the Norton, Water low and Braden Risk Assessment Tools. The Braden score was found to be most appropriate for the CABG population given its superior sensitivity (78%) and specificity (29%) at a cut-off point of 16. Remaining scores indicated that patients should all be considered as at risk for the first five postoperative days.

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A unique consideration after CABG surgery includes the impact of mental health on the post-operative complications. In a study of 135,701 CABG surgeries in the New York state database, patients with mental disorders (schizophrenia, major depression, dementia, bipolar disorder, and other psychiatric conditions) were found to have higher rates of PI than those without mental disorders (7.3/1000 vs. 1.8/1000; AOR 1.42, p=.006) (Li, Glance, Cai, & Mikael, 2008). Additionally, the effect of mental health disorders on patient safety varied widely between hospitals suggesting different facilities are not as adept as others to care for patients with mental disorders. In this study, the adjusted odds ratio (OR 1.32; p<0.01) suggest that having a psychiatric disorder alone increases the risk of complication following CABG.

In a prospective longitudinal study of 100 cardiac surgery patients in Spain, 18% of patients developed PI, yet no statistically significant variables were found to differentiate the PI and non-PI groups.[42] No relationship between the duration of surgery, cardiopulmonary bypass time, blood pressure or hypothermia and development of a PI was reported by the researchers.

A descriptive cross-sectional study of 333 patients in Iran [43] identified a 21.3% (n=71) PI incidence rate. Of these, 94% were identified immediately after the procedure, within the first 24 hours in ICU or after transferring to the general floor. Risk factors associated with PI development in multivariate analysis included age, gender, hypertension, myocardial infarction, intraoperative hypoxemia, not having a specialty mattress post operatively, blood pressure sustained less than 80mmHg systolic, requiring reoperation, low hematocrit, low albumin and increased length of hospital stay leading to increased PI risk.

In a study of 286 adult and pediatric cardiac surgery patients from China, the PI incidence rate in adults was 18.8%, with significant predictors of corticosteroid administration (p<0.05) and length of surgery (p=0.03)[44]. The authors' stated that cardiopulmonary bypass, gender, weight,

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intraoperative and post-operative vasoactive medications were not significant predictors of PI risk. In a separate prospective consecutive cohort study of 149 patients in a cardiac ICU in China [45], a 24.8% incidence rate of PI development was reported with 94.6% of identified as stage 1 and the remainder (5.4%) stage 2. Logistic regression indicated that valvular disease (OR 6.43, 95% CI 1.44, 28.69; p=0.063) coronary artery disease (OR 8.8, 95% CI 1.74, 44.62; p<0.03), weight (OR 0.971, 95%CI 0.94-1.004; p<0.084) and surgery duration (OR 1.005, 95%CI 1.000-1.010; p<0.036) were the major risk factors for ulceration. A primary limitation of this study was the author's use of the 2007 National Pressure Ulcer Advisory Panel (NPUAP) pressure ulcer staging definitions, yet inclusion of only Stages 1-4 PI as their method of classification. Therefore, it is possible that the high rate of reported stage 1 pressure injuries reflects the misclassification of deep tissue pressure injuries (DTPI).

Robich and colleagues investigated rates and risks associated with "never events" using the National Inpatient Database (NIS) between 2003 and 2011 for all patients undergoing adult cardiac operations, specifically looking at CABG, valve surgeries, and thoracic aneurysm repair [46]. The study included 588,417 patients among whom 4377 "never events" were reported. PI rates were reported as 4% over the entire study period, however, this number likely reflects historical bias as rates were reported as 0% between 2003-2007 and 12% between 2008-2011. The Centers for Medicare and Medicaid Services (CMS) decision to no longer reimburse hospitals for hospital acquired conditions such as PIs at a higher diagnostic category on October 1, 2008, likely resulted in the high rate of change between these two-time periods. However, the study did determine that cardiac surgery patients who experience a never event were at an increased risk of morality (OR 2.63, 95% CI 2.16-3.2, p<0.001), length of stay (MR 2.03, 95%CI 1.98-2.09, p<0.001) and total hospital charges (MR 1.73, 95% CI 1.68-1.78; p<0.001).

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Mixed Surgical Population

Mixed surgical patient studies were considered to identify other potential risk factors but adds selection bias due to variance in underlying comorbid states, operative body position and the lack of CPB for non-cardiac patients. Liu and associates (2012) performed a meta-analysis of six studies (4 cardiac surgery, 2 mixed surgical populations) of 2453 to investigate the effect of diabetes mellitus (DM) on the development of PIs during surgical procedures. The incidence rate across studies was 11.8%, with no significant heterogeneity (X^2_5 =1.98, p=0.85, I^2=0%) between the studies. All studies were listed as IIB evidence and 7/8 for quality according to the Newcastle-Ottawa scale. The meta-analysis revealed that DM was significantly associated with the development of PI (OR 2.15 (95%CI: 1.62-2.84; Z-5.32, p<0.00001, fixed effects model OR=2.13). Even after the removal of one retrospective study, the odds ratio was still significant (OR=2.03) [47]. These findings were supported by a second meta-analysis of 13 studies including total comparison groups of patients with PI (n=2367) and patients without (n=12053) showing DM to be a significant risk factor across surgical types with a pooled odds ratio of 1.74 (95%CI= 1.40-2.15, I^2=51.1%) [48]. When isolating the four studies involving cardiac surgery patients alone, DM remained a significant risk factor (OR=2.0, 95%CI=1.42-2.82, I^2= 0%). Importantly the authors identified an additional consideration in the cardiac surgery population to be limited movement associated with IABP and VAD devices, however these interventions modalities were not evaluated in the statistical model.

A systematic review of the literature by Rao and colleagues (2016) reviewed 12 studies looking at critical care, surgical ICU or cardiac surgery ICU for preoperative risks of PI development. The authors described significant risk factors according to preoperative, intraoperative and postoperative findings. The highest odds for PI development included spinal

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cord injury (OR 16.8), history of previous PI (OR 13.51), and hemodialysis within 24 and 48 hours of surgery (OR= 4.77; 9.43 respectively), DM (OR=2.70), fecal incontinence (OR 3.27) limited mobility (4.42), and mechanical ventilation (OR=4.82) The researchers highlighted the relative absence of DTPI in the studies in this review and suggested that "hypoxic reperfusion" is linked to DTPI and has not been sufficiently included in previous frameworks of PI development. Articles addressing DTPI include a 5 year retrospective study of 119 patients in a seven surgical ICUs [49]. The authors found that for every hour the patient spent in surgery, the risk of DTPI increased by 20%. Other significant variables included dialysis (OR 4.0, 95%CI 06-0.99, p=0.05), cardiogenic/septic shock (OR=10, 95%CI 0.025-0.43, p=0.002), low diastolic blood pressure (OR 0.93, 95%CI 0.88-0.99, p=0.02) and time of surgery in hours (OR 1.20, 95% 1.07-1.33, p=0.001). Cox and Roche (2015) identified an incidence of 13% (41/306) in a retrospective correlational study of 306 patients in a medical surgical and cardiac surgical ICU [50]. Of these pressure injuries, 39% were DTPI and 56% were found on the sacrum. The authors identified significant risk factors for PI development included longer infusion times of: vasopressin (32 hours vs 87 hours, p=0.005), high dose vasopressin (20 hours vs. 57 hours, p=0.03) and patients receiving both vasopressin and norepinephrine (X^2=39.3, p<0.001). Vasopressin was the only vasoactive medication to emerge as a significant predictor in multivariate analysis. The authors commented that the dose of 0.03 U/min at longer infusion times may be a tipping point for pressure injury development.

A retrospective matched case-control study of 32,963 patients from a level-one trauma center in the US investigated the time in the operating room as a risk factor for PI.[51] In this study there was an overall 2.8% incidence rate and time in surgery was identified as a significant risk with increasing odds over time (<2 hours OR=1.1; 2-4 hours OR=1.2; 4-6 hours OR= 1.6; >6 hours OR 6.4). Additionally, documentation of PI occurrence 72 hours after surgery was found in 78%

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of patients, with only 4.5% present within the first 24 hours, suggesting an extended assessment period after surgery is necessary for PI identification [52]. A prospective convenience sample of 258 patients undergoing operations of 3 hours or more (21/258 cardiac; 69/258 general surgery) found a PI incidence rate of 8.1% overall [53]. Significant risk factors identified in logistic regression included use of specific Operating Room table pads: foam pad (OR=14.740), OR table with Foam pad and valve (OR=3.397), use of gel pad on the OR table (OR=2.809), use of the Jackson table (OR 2.231) and preoperative patient temperature (OR 1.014). Of those patients who developed PI, 33.7% of the PI group had ASA scores of 2, while 53.5% had ASA scores of 3. The use of ASA scores to identify risk is further supported by a retrospective secondary analysis of 2695 patients from cardiovascular, burn and surgical ICUs reported a 10% PI incidence rate and identified ASA score of 4 or 5 [26] as a significant predictor of PI development. Propensity matching of 122 cases identified a significant intraoperative risk factor to be receipt of blood products (OR 1.71, 95%CI, 1.03-2.84, p=0.04).

DISCUSSION

The cardiac surgery population has historically been identified with intraoperative PI incidence rates as high as 29.5%, [11,54]. Subsequent prospective cohort studies of subpopulations such as cardiac surgery bypass grafting (CABG), the most commonly studied cardiac surgical intervention, have shown incidence rates as high as 53.4% in the cardiac ICU [55] yet the actual incidence and prevalence is still unknown. One of the greatest limitations of available literature reviews and research in the cardiac surgery population is the preponderance of these earlier studies occurring prior to the description and recognition of deep tissue pressure injuries (DTPI) (Black, Brindle, & Honaker, 2016). Review of articles prior to inclusion of DTPI in National Pressure Ulcer Advisory Panel Guidelines in 2007 [39] would lead to historical bias. For example, three studies commented

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on "violet pressure ulcer" (Feuchtinger et al., 2005), ecchymosis as a risk factor for PI [14] and in Schoonhoven and colleagues' study, 34 patients were excluded due to symptoms that were not common to known PI staging classifications systems at the time [16]. The authors described, "painful or numb discoloration that disappeared (partially) when light pressure was applied; sharply defined; indurated; lasting 13-21 days despite relief of pressure, and/or bright red discoloration." (p.169). These inconsistencies in assessment likely led to misclassification of many post-operative PI prior to 2007 given the high rate of reported stage 1 and stage 2 PI in these early studies.

Additionally, an important consideration that is not addressed in the studies regarding PI etiology to date is the distinction between pulsatile versus non-pulsatile blood flow both during CPB intraoperatively and during the use of VAD devices in the postoperative period. Intraoperatively, non-pulsatile blood flow, theoretically, may not provide sufficient intravascular pressure to open the dermal capillary sphincters, possibly impacting cutaneous vascularization. Moreover, during CPB, the impact of volumetric dilution of the circulating serum on perfusion of the cutaneous complex is not well understood. Contrasting the concern over pulseless blood flow during CPB, is the understanding that patients with VAD devices who are ambulatory after surgery, do not have spontaneous cutaneous vascular collapse despite being on an ongoing pulseless flow device.

Animal research investigating the concerns over end organ perfusion between pulsatile and non-pulsatile circulation has been described. A porcine study of 20 pigs randomized to 4 groups (pulseless and pulsatile groups at two different pressure settings evaluated within the renal artery) were evaluated for impact of perfusion on renal recovery following normothermic ischemia [57]. In the high pressure pulseless and pulsatile groups (renal artery pressure 65 ± 1.6 mmHg) no differences were seen in renal recovery. However, in the lower pressure groups (40 ± 1.1 mmHg)

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there was a significant difference in recovery of renal blood flow, ATP recovery and VO2, with pulsatile perfusion being superior to pulseless perfusion in all outcomes. Further, results indicated no difference in renal histology between the pulseless or pulsatile groups. A later study reported the impact of end-organ function during chronic non-pulsatile circulation using an animal model of 15 sheep allocated to LVAD or control group which were sacrificed electively at 30, 90, 180 and 340 days for evaluation [58]. The researchers report that there were no histologic differences between organs of pulsatile and non-pulsatile animals, no significant difference in mean blood pressure, however significantly elevated plasma renin levels in pulseless animals was found. Feng and colleagues evaluated the short-term effects of completely non-pulsatile versus pulsatile circulation on peripheral vascular permeability of 10 calves with continuous flow Heartmate III rotary pumps [59]. Five calves had their pump speeds modulated to result in a low frequency pulse pressure of 10-25mmhg (physiologic range) at 40 pulses a minute, while the remaining five had non-pulsatile systemic circulation. Researchers assessed skeletal muscle biopsies at postoperative days 1, 7 and 14 with additional comparisons of tissue water content, morphologic alterations and comparisons of immunohistochemistry in respective biopsies. Results indicated no significant differences in tissue water content, or skeletal muscle morphology at any postoperative time point. There were no significant differences in the expression or distribution of study immunohistochemical biomarkers between the groups causing researchers to observe no peripheral endothelial injury or peripheral microvascular permeability in either group. These animal studies, therefore, raise the question as to whether pulseless blood flow alone is a risk factor for PI development or is systemic inflammatory response associated with total CBP time more associated with downstream impact to end tissue perfusion?

LIMITATIONS

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First, as there were no articles identified in the literature for VAD-TAH surgery patients and PI, there is inherent risk of selection bias in the creation of the secondary search string as the author attempted to select a surgical population that approximated the risks associated with VAD-TAH procedures, namely, on-pump cardiac surgery.

There is considerable probability that many Stage 1 PI and stage 2 PI reported in these studies were actually deep tissue injury, which greatly changes the severity of the injury itself. This fact was highlighted in the study by Cox and Roche (2015) as their results contrasted historical outcomes with 39% of the observed pressure injuries being DTPI with 56% of them found on the sacrum. Another possible explanation for this difference in reported severity may be the overall morbidity of patients and advanced, life-prolonging intensive care management in 2017 versus the studies of the early 1990s.

CONCLUSION

The incidence and natural history of PI development in the VAD and TAH cardiac surgery patient remains unknown. This finding represents a significant gap in our understanding of pressure injury etiology and prevention warranting on-going research. Additionally, a systematic review of 1533 articles failed to identify studies specifically investigating interventions for PI prevention in the cardiac surgery population [60]. This gap in existing evidence does little to reduce the risk and rate of PI in cardiac surgery patients [54] and highlights the critical need to identify risk factors leading to PI development to guide prevention in the cardiac surgery population. The systematic review reported here will guide the first, 8-year retrospective analysis of VAD and TAH patients to identify incidence, and predictors of PI development in a large academic university health center in the United States.

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REFERENCES

1. Haesler E. National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, Pan Pacific Pressure Injury Alliance: Guidelines for the Prevention and Treatment of Pressure Ulcers. Perth, Australia; 2014.

2. Edsberg LE, Black JM, Goldberg M, McNichol L, Moore L, Sieggreen M. Revised National Pressure Ulcer Advisory Panel Pressure Injury Staging System: Revised Pressure Injury

www.manaraa.com

Staging System. J Wound Ostomy Cont Nurs Off Publ Wound Ostomy Cont Nurses Soc. 2016;43(6):585-597. doi:10.1097/WON.0000000000000281

3. Vangilder C, Macfarlane GD, Meyer S. Results of nine international pressure ulcer prevalence surveys: 1989 to 2005. Ostomy Wound Manage. 2008;54(2):40-54.

4. The Joint Commission. Strategies for Preventing Pressure Ulcers. Jt Comm Perspect Patient Saf. 2008;8(1):5-7.

5. Padula WV, Delarmente BA. The national cost of hospital-acquired pressure injuries in the United States. Int Wound J. 2019;16(3):634-640. doi:10.1111/iwj.13071

6. Kurtzman ET, Buerhaus PI. New Medicare payment rules: danger or opportunity for nursing? Am J Nurs. 2008;108(6):30-35. doi:10.1097/01.NAJ.0000324370.71532.b7

7. Padula WV, Mishra MK, Makic MBF, Sullivan PW. Improving the quality of pressure ulcer care with prevention: a cost-effectiveness analysis. Med Care. 2011;49(4):385-392. doi:10.1097/MLR.0b013e31820292b3

8. Russo CA, Steiner C, Spector W, Agency for Healthcare Research and Quality. Hospitalizations Related to Pressure Ulcers. HCUP Statistical Brief #64. 2008. http://www.hcup-us.ahrq.gov/reports/statbriefs/sb64.pdf.

9. University Healthcare Consortium. Guide for change-pressure ulcers [Webinar]. http://www.uhc.edu/33468. Accessed March 10, 2010.

10. Aronovitch SA. Intraoperatively acquired pressure ulcer prevalence: a national study. J Wound Ostomy Cont Nurs Off Publ Wound Ostomy Cont Nurses Soc. 1999;26(3):130-136.

www.manaraa.com

11. Feuchtinger J, Halfens RJG, Dassen T. Pressure ulcer risk factors in cardiac surgery: a review of the research literature. Heart Lung J Crit Care. 2005;34(6):375-385. doi:10.1016/j.hrtlng.2005.04.004

12. Kemp MG, Keithley JK, Smith DW, Morreale B. Factors that contribute to pressure sores in surgical patients. Res Nurs Health. 1990;13(5):293-301.

13. Lewicki LJ, Mion L, Splane KG, Samstag D, Secic M. Patient risk factors for pressure ulcers during cardiac surgery. AORN J. 1997;65(5):933-942.

14. Papantonio CT, Wallop JM, Kolodner KB. Sacral ulcers following cardiac surgery: incidence and risks. Adv Wound Care J Prev Heal. 1994;7(2):24-36.

15. Pokorny ME, Koldjeski D, Swanson M. Skin care intervention for patients having cardiac surgery. Am J Crit Care Off Publ Am Assoc Crit-Care Nurses. 2003;12(6):535-544.

16. Schoonhoven L, Defloor T, van der Tweel I, Buskens E, Grypdonck MHF. Risk indicators for pressure ulcers during surgery. Appl Nurs Res ANR. 2002;15(3):163-173.

17. Stordeur S, Laurent S, D'Hoore W. The importance of repeated risk assessment for pressure sores in cardiovascular surgery. J Cardiovasc Surg (Torino). 1998;39(3):343-349.

18. Lyder CH, Ayello EA. Pressure Ulcers: A Patient Safety Issue. In: Hughes RG, ed. Patient Safety and Quality: An Evidence-Based Handbook for Nurses. Advances in Patient Safety. Rockville (MD): Agency for Healthcare Research and Quality (US); 2008. http://www.ncbi.nlm.nih.gov/books/NBK2650/. Accessed September 6, 2016.

www.manaraa.com

19. VanGilder C, Amlung S, Harrison P, Meyer S. Results of the 2008-2009 International Pressure Ulcer Prevalence Survey and a 3-year, acute care, unit-specific analysis. Ostomy Wound Manage. 2009;55(11):39-45.

20. Silva Enciso J. Mechanical Circulatory Support: Current Status and Future Directions. Prog Cardiovasc Dis. 2016;58(4):444-454. doi:10.1016/j.pcad.2016.01.006

21. Allen LA, Smoyer Tomic KE, Wilson KL, Smith DM, Agodoa I. The inpatient experience and predictors of length of stay for patients hospitalized with systolic heart failure: comparison by commercial, Medicaid, and Medicare payer type. J Med Econ. 2013;16(1):43-54. doi:10.3111/13696998.2012.726932

22. Colvin M, Smith JM, Skeans MA, et al. Heart. Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg. 2016;16 Suppl 2:115-140. doi:10.1111/ajt.13670

23. Cotts WG, McGee EC, Myers SL, et al. Predictors of hospital length of stay after implantation of a left ventricular assist device: An analysis of the INTERMACS registry. J Heart Lung Transplant. 2014;33(7):682-688. doi:10.1016/j.healun.2014.02.022

24. El Banayosy A, Kizner L, Arusoglu L, et al. Home Discharge and Out-of-Hospital Follow-Up of Total Artificial Heart Patients Supported by a Portable Driver System. Asaio J. 2014 ;60(2) :148-153. doi:10.1097/MAT.0000000000000046

25. Dripps RD, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. JAMA. 1961;178:261-266.

www.manaraa.com

26. O'Brien DD, Shanks AM, Talsma A, Brenner PS, Ramachandran SK. Intraoperative risk factors associated with postoperative pressure ulcers in critically ill patients: a retrospective observational study. Crit Care Med. 2014;42(1):40-47. doi:10.1097/CCM.0b013e318298a849

27. Esper SA, Subramaniam K, Tanaka KA. Pathophysiology of Cardiopulmonary Bypass: Current Strategies for the Prevention and Treatment of Anemia, Coagulopathy, and Organ Dysfunction. Semin Cardiothorac Vasc Anesth. 2014;18(2):161-176. doi:10.1177/1089253214532375

28. Braun JP, Buhner S, Kastrup M, et al. Barrier function of the gut and multiple organ dysfunction after cardiac surgery. J Int Med Res. 2007;35(1):72-83. doi:10.1177/147323000703500107

29. Jarral OA, Saso S, Harling L, et al. Organ dysfunction in patients with left ventricular impairment: what is the effect of cardiopulmonary bypass? Heart Lung Circ. 2014;23(9):852-862. doi:10.1016/j.hlc.2014.03.012

30. Ruel M, Khan TA, Voisine P, Bianchi C, Sellke FW. Vasomotor dysfunction after cardiac surgery. Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg. 2004;26(5):1002-1014. doi:10.1016/j.ejcts.2004.07.040

31. Lundemoen S, Kvalheim VL, Svendsen ØS, et al. Intraaortic counterpulsation during cardiopulmonary bypass impairs distal organ perfusion. Ann Thorac Surg. 2015;99(2):619-625. doi:10.1016/j.athoracsur.2014.08.029

32. Murphy GJ, Angelini GD. Side effects of cardiopulmonary bypass: what is the reality? J Card Surg. 2004;19(6):481-488. doi:10.1111/j.0886-0440.2004.04101.x

www.manaraa.com

33. Wan S, Yim APC, Ng CSH, Arifi AA. Systematic organ protection in coronary artery surgery with or without cardiopulmonary bypass. J Card Surg. 2002;17(6):529-535.

34. Song Y, Soh S, Shim J-K, Park K-U, Kwak Y-L. Skin perfusion pressure as an indicator of tissue perfusion in valvular heart surgery: Preliminary results from a prospective, observational study. PloS One. 2017;12(9):e0184555. doi:10.1371/journal.pone.0184555

35. Moher D, Liberati A, Tetzlaff J, Altman D. The Prisma Group: Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097

36. Newhouse R, Dearholt S, Poe S, Pugh L, White K. The Johns Hopkins Nursing Evidence-based Practice Rating Scale. 2005.

37. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 Chapter 8: Assessing Risk of Bias in Included Studies. http://methods.cochrane.org/bias/assessing-risk-bias-included-studies. Published 2011. Accessed November 8, 2017.

38. Kirklin JK, Naftel DC. Mechanical Circulatory Support: Registering a Therapy in Evolution. Circ Heart Fail. 2008;1(3):200-205. doi:10.1161/CIRCHEARTFAILURE.108.782599

39. Black J, Baharestani MM, Cuddigan J, et al. National Pressure Ulcer Advisory Panel's updated pressure ulcer staging system. Adv Skin Wound Care. 2007;20(5):269-274. doi:10.1097/01.ASW.0000269314.23015.e9

40. de Jaegere PPT, Suyker WJL. Off-pump coronary artery bypass surgery. Heart. 2002;88(3):313-318.

www.manaraa.com

41. Li Y, Glance LG, Cai X, Mukamel DB. Adverse hospital events for mentally ill patients undergoing coronary artery bypass surgery. Health Serv Res. 2008;43(6):2239-2252. doi:10.1111/j.1475-6773.2008.00875.x

42. Gómez Ginés D, Rodríguez Palma M, García Pavón F, Almozara Molle R, Torra i Bou JE. Úlceras por presión en quirófano: Incidencia intraoperatoria en pacientes sometidos a cirugía cardíaca. Gerokomos. 2009;20(4):176-180.

43. Alizadeh Ghavidel A, Bashavard S, Bakhshandeh Abkenar H, Payghambari MM. Incidence rate of pressure sores after cardiac surgery during hospitalization and its relevant factors. RJMS. 2012;19(102):18-29.

44. Shen W-Q, Chen H-L, Xu Y-H, Zhang Q, Wu J. The Relationship Between Length of Surgery and the Incidence of Pressure Ulcers in Cardiovascular Surgical Patients: A Retrospective Study. Adv Skin Wound Care. 2015;28(10):444-450. doi:10.1097/01.ASW.0000466365.90534.b0

45. Lu C-X, Chen H-L, Shen W-Q, Feng L-P. A new nomogram score for predicting surgery-related pressure ulcers in cardiovascular surgical patients. Int Wound J. 2017;14(1):226-232. doi:10.1111/iwj.12593

46. Robich MP, Krafcik BM, Shah NK, Farber A, Rybin D, Siracuse JJ. Analysis of "never events" following adult cardiac surgical procedures in the United States. J Cardiovasc Surg (Torino). 2017;58(5):755-762. doi:10.23736/S0021-9509.17.09866-4

47. Liu P, He W, Chen H-L. Diabetes mellitus as a risk factor for surgery-related pressure ulcers: a meta-analysis. J Wound Ostomy Cont Nurs Off Publ Wound Ostomy Cont Nurses Soc. 2012;39(5):495-499. doi:10.1097/WON.0b013e318265222a

www.manaraa.com

48. Kang Z-Q, Zhai X-J. The Association between Pre-existing Diabetes Mellitus and Pressure Ulcers in Patients Following Surgery: A Meta-analysis. Sci Rep. 2015;5:13007. doi:10.1038/srep13007

49. Kirkland-Kyhn H, Teleten O, Wilson M. A Retrospective, Descriptive, Comparative Study to Identify Patient Variables That Contribute to the Development of Deep Tissue Injury Among Patients in Intensive Care Units. Ostomy Wound Manage. 2017;63(2):42-47.

50. Cox J, Roche S. Vasopressors and development of pressure ulcers in adult critical care patients. Am J Crit Care Off Publ Am Assoc Crit-Care Nurses. 2015;24(6):501-510. doi:10.4037/ajcc2015123

51. Hayes RM, Spear ME, Lee SI, et al. Relationship between time in the operating room and incident pressure ulcers: a matched case-control study. Am J Med Qual Off J Am Coll Med Qual. 2015;30(6):591-597. doi:10.1177/1062860614545125

52. Hayes RM, Spear ME, Lee SI, et al. Relationship between time in the operating room and incident pressure ulcers: a matched case-control study. Am J Med Qual Off J Am Coll Med Qual. 2015;30(6):591-597. doi:10.1177/1062860614545125

53. Primiano M, Friend M, McClure C, et al. Pressure ulcer prevalence and risk factors during prolonged surgical procedures. AORN J. 2011;94(6):555-566. doi:10.1016/j.aorn.2011.03.014

54. Rao AD, Preston AM, Strauss R, Stamm R, Zalman DC. Risk Factors Associated with Pressure Ulcer Formation in Critically Ill Cardiac Surgery Patients: A Systematic Review. J Wound Ostomy Cont Nurs Off Publ Wound Ostomy Cont Nurses Soc WOCN. 2016;43(3):242-247. doi:10.1097/WON.0000000000000224

www.manaraa.com

55. Schuurman J-P, Schoonhoven L, Keller BPJA, van Ramshorst B. Do pressure ulcers influence length of hospital stay in surgical cardiothoracic patients? A prospective evaluation. J Clin Nurs. 2009;18(17):2456-2463. doi:10.1111/j.1365-2702.2008.02711.x

56. Black JM, Brindle CT, Honaker JS. Differential diagnosis of suspected deep tissue injury. Int Wound J. 2016;13(4):531-539. doi:10.1111/iwj.12471

57. Konishi H, Yland MJ, Brown M, et al. Effect of pulsatility and hemodynamic power on recovery of renal function. ASAIO J Am Soc Artif Intern Organs 1992. 1996;42(5):M720-723.

58. Saito S, Westaby S, Piggot D, et al. End-organ function during chronic nonpulsatile circulation. Ann Thorac Surg. 2002;74(4):1080-1085.

59. Feng J, Cohn WE, Parnis SM, et al. New continuous-flow total artificial heart and vascular permeability. J Surg Res. 2015;199(2):296-305. doi:10.1016/j.jss.2015.06.035

60. Ettema RGA, Van Koeven H, Peelen LM, Kalkman CJ, Schuurmans MJ. Preadmission interventions to prevent postoperative complications in older cardiac surgery patients: a systematic review. Int J Nurs Stud. 2014;51(2):251-260. doi:10.1016/j.ijnurstu.2013.05.011

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FIGURE 1. John's Hopkins Nursing Evidence-based Practice Rating Scale

JHNEBP EVIDENCE RATING SCALES

STRENGTH of the Evidence	
Level I	Experimental study/randomized controlled trial (RCT) or meta analysis of RCT
Level II	Quasi-experimental study
Level III	Non-experimental study, qualitative study, or meta-synthesis.
Level IV	Opinion of nationally recognized experts based on research evidence or expert consensus panel (systematic review, clinical practice guidelines)
Level V	Opinion of individual expert based on non-research evidence. (Includes case studies; literature review; organizational experience e.g., quality improvement and financial data; clinical expertise, or personal experience)

QUALITY of the Evidence		
A High	Research	consistent results with sufficient sample size, adequate control, and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence.
	Summative reviews	well-defined, reproducible search strategies; consistent results with sufficient numbers of well defined studies; criteria-based evaluation of overall scientific strength and quality of included studies; definitive conclusions.
	Organizational	well-defined methods using a rigorous approach; consistent results with sufficient sample size; use of reliable **and** valid measures
	Expert Opinion	expertise is clearly evident
B Good	Research	reasonably consistent results, sufficient sample size, some control, with fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence
	Summative reviews	reasonably thorough and appropriate search; reasonably consistent results with sufficient numbers of well defined studies; evaluation of strengths and limitations of included studies; fairly definitive conclusions.
	Organizational	Well-defined methods; reasonably consistent results with sufficient numbers; use of **reliable and valid** measures; reasonably consistent recommendations
	Expert Opinion	expertise appears to be credible.
C Low quality or major flaws	Research	little evidence with inconsistent results, insufficient sample size, conclusions cannot be drawn
	Summative reviews	undefined, poorly defined, or limited search strategies; insufficient evidence with inconsistent results; conclusions cannot be drawn
	Organizational	Undefined, **or** poorly defined methods; insufficient sample size; inconsistent results; undefined, poorly defined or measures that lack adequate reliability or validity
	Expert Opinion	expertise is not discernable or is dubious.

**A study rated an A would be of high quality, whereas, a study rated a C would have major flaws that raise serious questions about the believability of the findings and should be automatically eliminated from consideration.*

Newhouse R, Dearholt S, Poe S, Pugh LC, White K. The Johns Hopkins Nursing Evidence-based Practice Rating Scale. 2005. Baltimore, MD, The Johns Hopkins Hospital; Johns Hopkins University School of Nursing.

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FIGURE 2. Search Strategy for Systematic Review of VAD-TAH Patients

VAD-TAH String 1

(((((("Heart Failure"[Mesh] OR Heart Failure[TIAB])) OR (("Cardiovascular Surgical Procedures"[Mesh] OR Cardiovascular Surgical Procedure*[TIAB])) OR (((((("Vascular Assist Device*[TIAB] OR Artificial Ventricle*[TIAB] OR Heart Assist Pump*[TIAB] OR Heart Assist Device*[TIAB] OR Ventricular Assist Device*[TIAB] OR Artificial Heart Ventricle*[TIAB] OR Artificial Heart*[TIAB])) OR (((((("Heart, Artificial"[Mesh]) OR Artificial Heart[TIAB])) OR ((Implantable Device*[TIAB]) AND (Heart patient*[TIAB] OR Cardiac Patient*[TIAB])))) OR (("Heart-Assist Devices"[Mesh] OR "Heart, Artificial"[Mesh])) OR (((Device*[TIAB])) AND ((Heart Lung Bypass*[TIAB] OR Cardiopulmonary Bypass*[TIAB])))) OR "Cardiopulmonary Bypass"[Mesh])) AND ((("Pressure/adverse effects"[Mesh]) OR Deep Tissue Injur*[TIAB]) OR (("Pressure Ulcer"[Mesh] OR Pressure Ulcer*[TIAB] OR Bedsore*[TIAB] OR Pressure Sore*[TIAB] OR Decubitus Ulcer*[TIAB] OR Bed Sore*[TIAB])) Filters: English

VAD-TAH String 2

(((((("Heart Failure"[Mesh] OR Heart Failure[TIAB])) OR (("Cardiovascular Surgical Procedures"[Mesh] OR Cardiovascular Surgical OR “Operating Room” OR “Operating Theatre” OR “Intraoperative” OR Procedure*[TIAB])) OR (((((("Vascular Assist Device*[TIAB] OR Artificial Ventricle*[TIAB] OR Heart Assist Pump*[TIAB] OR Heart Assist Device*[TIAB] OR Ventricular Assist Device*[TIAB] OR Artificial Heart Ventricle*[TIAB] OR Artificial Heart*[TIAB])) OR (((((("Heart, Artificial"[Mesh]) OR Artificial Heart[TIAB])) OR ((Implantable Device*[TIAB]) AND (Heart patient*[TIAB] OR Cardiac Patient*[TIAB])))) OR (("Heart-Assist Devices"[Mesh] OR "Heart, Artificial"[Mesh])) OR (((Device*[TIAB])) AND ((Heart Lung Bypass*[TIAB] OR Cardiopulmonary Bypass*[TIAB])))) OR "Cardiopulmonary Bypass"[Mesh])) AND ((("Pressure/adverse effects"[Mesh]) OR Deep Tissue Injur*[TIAB]) OR (("Pressure Ulcer"[Mesh] OR Pressure Ulcer*[TIAB] OR Bedsore*[TIAB] OR Pressure Sore*[TIAB] OR Decubitus Ulcer*[TIAB] OR Bed Sore*[TIAB]))

CARDIAC SURG, NO-DEVICE 1

(((((("Heart Failure"[Mesh] OR Heart Failure[TIAB])) OR (("Cardiovascular Surgical Procedures"[Mesh] OR Surgery OR Cardiovascular Surgical Procedure*[TIAB])) AND Intraoperative AND (Heart patient*[TIAB] OR Cardiac Patient*[TIAB])))) OR ((Heart Lung Bypass*[TIAB] OR “on-pump” [TIAB] OR Cardiopulmonary Bypass*[TIAB])))) OR "Cardiopulmonary Bypass"[Mesh])) AND ((("Pressure/adverse effects"[Mesh]) OR Deep Tissue Injur*[TIAB]) OR (("Pressure Ulcer"[Mesh] OR Pressure Ulcer*[TIAB] OR Bedsore*[TIAB] OR Pressure Sore*[TIAB] OR Decubitus Ulcer*[TIAB] OR Bed Sore*[TIAB])) Filters: English

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FIGURE 3. Flow Diagram of Systematic Review

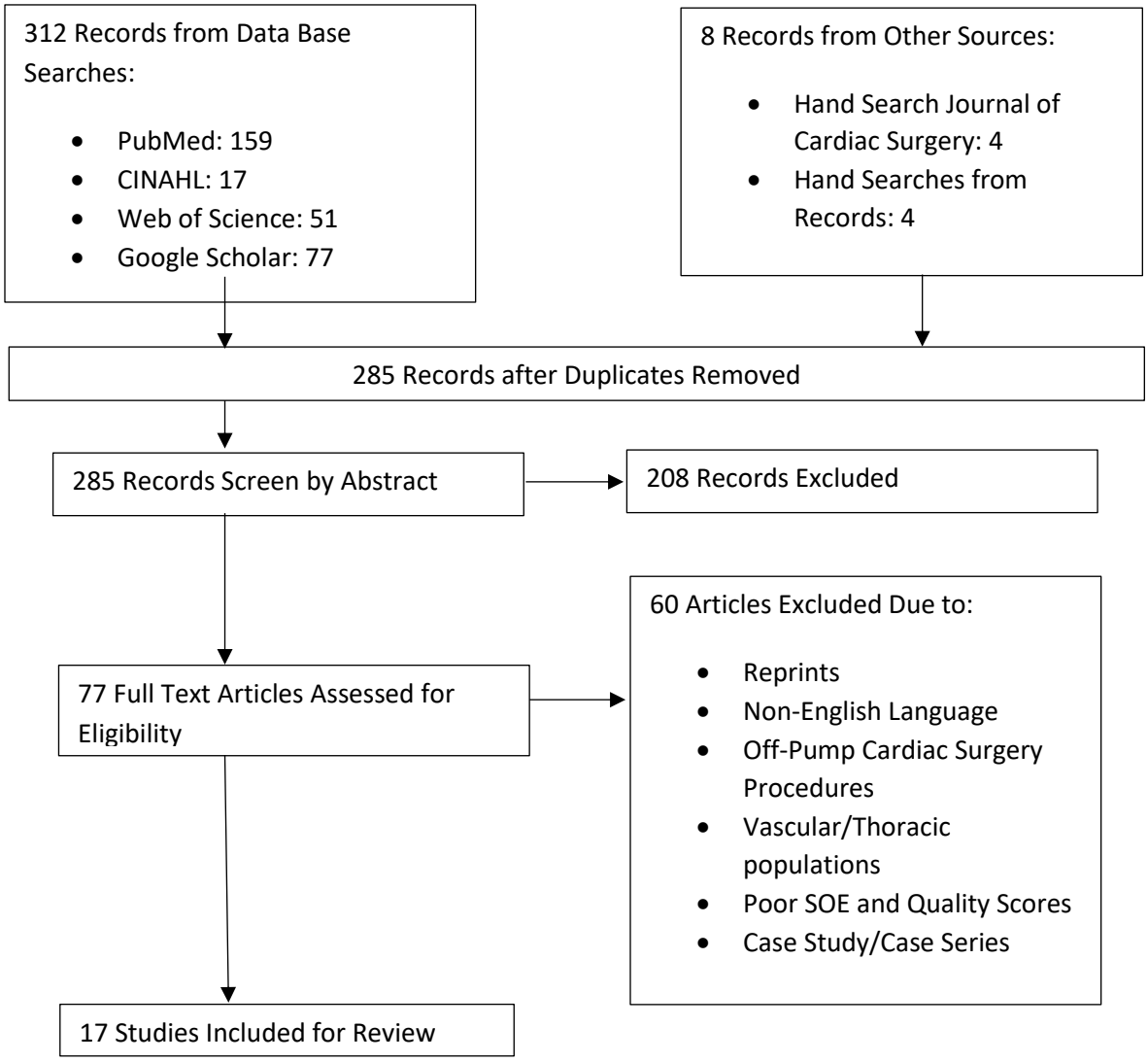

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TABLE 1: Cardiopulmonary Bypass Systemic Inflammatory Response

Inflammatory Response Secondary to CPB	**Author**
Activation of complement secondary to contact with CPB circuits and formation of anaphylatoxins and terminal membrane attack complex (C5b-C9).	Esper, et al 2014; Murphy & Angelini, 2004;
Autonomic regulation of peripheral and myocardial arterioles; decreased peripheral vascular resistance on separation from CPB.	Ruel, et al 2004; Song et al, 2017.
Neutrophil activation from anaphylatoxins and kallikreins causing lytic enzyme release and reactive oxygen species.	Ruel, et al 2004; Murphy & Angelini, 2004; Esper et al, 2014;
Cytokine activation increasing inflammation and ROS response and endotoxin production.	Esper, et al 2014;
Metabolic derangement of hyperglycemia, hyperinsulinemia and insulin resistance.	Ruel et al, 2004; Esper, et al 2014;
Profibrinolytic state: elevated tissue plasminogen activator (tPA)	Esper, et al 2014;
Hemodilution leading to decreased oxygen carrying capacity and tissue ischemia.	Wan, et al 2002; Esper et al, 2014;
Ischemia Reperfusion Injury: intracellular calcium trapping, reactive oxygen species and neutrophil-endothelium interactions. Causes access synthesis of superoxides, hydroxyl radicals and peroxynitrate free radicals.	Ruel et al, 2004; Wan et al, 2002;
Embolic events: gaseous, lipoproteins and particulate.	Murphy & Angelini, 2004
Leukocyte Production: causes neutrophil rolling, adherence and transmigration with increased lifespan. Leads to infiltration.	Murphy & Angelini, 2004; Ruel et al, 2004;
Cyclooxygenase and constrictive prostaglandin release	Ruel, et al 2004;

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TABLE 2: Evidence Table

Study Author	Design	Strength of Evidence & Quality	Sample/Setting	Study Aim	PI Incidence & Prevalence	Predictors by Multivariate Analysis	Limitations
Feuchtinger, Halfens & Dassen, 2007	Prospective Observational, Convenience Sample	III B	53 Cardiac surgery patients (Germany) ICU Daily Assessment x4 days	To appraise risk assessment using a standardized instrument.	49%- 26/53 on POD 0 2 on POD 1 4 on POD 2 1 on POD 3 0 on POD 4 1 on POD 7 33 or 34 PI in this study… thought 33 from the text.	No multivariate analysis. Sensitivity/Specificity and design of Braden found to best fit CT Surgery population.	Attrition each day (total patients) POD1=53, POD2=36, POD3=20, POD4=17
Li, et al 2008	Retrospective Mental Disorder & Complications after CABG	III A	N=135,701 CABG in NY State Database (US) OR/ICU/Ward	Compare occurrence of postoperative complication in patients with and without	PI w/Mental Disorder 7.3/1000; without 1.8/1000	Decubitus ulcer AOR 1.42 (95%CI 1.10-1.82) p=0.006 Effect of mental disorders on safety	Authors suggest differing ability to care for psychiatric pts was hospital site dependent.

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				mental disorders who underwent CABG surgery in NY.		outcomes varied across hospitals (variance of random coefficients 0.16, SE=0.07 for overall complication; 0.79 SE=0.35 for PI. OR 1.32 (p<0.01) for psychiatric disorder alone having increased risk complication.	Mental disorders included: schizophrenia, major depression, bipolar, dementia, and other mental disorders by ICD-9 code.
Ginés, et al 2009	Prospective Longitudinal	III B	100 CT Surg (Spain) OR		18% (18 pts developed 22 PI) 10% had PI Stg 1 on arrival to OR.	No statistically sig variables found between PI and no PI group	No relationship of PI to duration of surgery, cardiopulmonary bypass time, BP or hypothermia.
Primiano, et al, 2011	Prospective observational, convenience sample	III B	258 patients with OR >3 hrs.	Identify prevalence of and risk factors associated with PI formation in	21/258 (8.1%)	Logistic regression: Foam Pad (OR=14.74) Gel Pad (OR=2.809)	ASA 2 (33.7% of PI) ASA 3 ((53.5%)

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			Cardiothoracic 21/258 General 69/258	the OR in patients undergoing surgery >3 hr.		Jackson Table (OR=2.231) Preop Temperature (1.014)	No significance: Type anesthesia, surgery, Surgery Length, intraop hypotension/hypoxia, not sig.
Ghavidel et al, 2012	Descriptive Cross-Sectional	III B	333 Patients (Iran) Cardiac Surgery OR and ICU		21.3% (71 PI, 67 in ICU, 4 after transfer ward).	Age, sex, HTN, MI, intraop hypoxemia, mattress, post op inotropes, BP <80mmhg, reoperation, low HCT, LOS, Low Albumin All significant in LR?	Most (what is the n/%) PI found immediately after OR within first 24 hours of ICU.
Liu, He, & Chen, 2012	Meta-analysis	IA	N=2453 (5 US, 1 Belgium) 6 Studies all listed as 2B evidence. 4/6 were cardiac surgery	Aim of meta-analysis was to review evidence related to association between DM and surgery related PI.	11/8% 290/2453 No sig heterogenicity (X^2_5 =1.98, p=0.85, I^2=0%)across studies	DM OR 2.15 (95%CI: 1.62-2.84; Z-5.32, p<0.00001) Fixed effects model DM OR 2.13 Removal of 1 Retro study OR 2.03 (for risk factor DM?)	No evidence of publication bias. All studies scored 7/8 on Newcastle-Ottawa scale for quality (what kind of quality?).

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			or included cardiac				
O'Brien, et al 2013	Retrospective Secondary Analysis	III A	2,695 patients from 3 ICUs Surgical ICU Burn ICU Cardiovascular ICU Merged datasets from Talsma et al and intraop database.	Hypothesized intraoperative risk factors increased likelihood of postoperative new-onset PI. Retrospective review to characterize intraoperative risk factors associated with development of PI.	10.7% (288/2695)	Independent predictors: ASA score 4 or 5; Underweight BMI, noncardiac operation, history of CHF, renal disease, existing airway prior to OR	9.7% stg 2, 0.8% stg 3, 0.4% stg 4, 23, 0.9% DTI 3.3% US. Propensity matching of 122 cases: Intra-operative blood products (OR 1.71, 95S%CI, 1.03-2.84, p-0.04); Pts. With PI: 60 minutes longer OR time(non-significant finding)
Ettema et al, 2013	Systematic Review of Lit (PRISMA)	III A	23 Studies (strict Inclusion) All studies B- to A+ Quality Score	To provide an overview of both single and multi-component preadmission interventions designed to prevent single	No studies Identified that described PI prevention.	NA No studies with PI as outcome variable	Authors conclude no high-quality evidence to prevent PI to date.

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				and multiple postoperative complications in older cardiac surgery patients.			
Hayes, et al, 2015	Retrospective, matched case-control.	III A	32,963 patients (Vanderbilt, USA) OR, ICU	To determine if time in the operating room increases risk of newly documented PI.	931/32,963 (2.8%)	OR for PI development and OR time: 1.1 <2hrs 1.2 >2, <4 1.6 >4, <6 6.4 >6 78% HAPU doc on POD3. 4.5% reported within 24hrs after OR.	NOTE: Pts with PI documented in first 24hrs deemed POA, but no description of pts admitted directly to OR, resulting in potentially missed PI.
Shen et al 2015	Retrospective Study with propensity score matching	III A	286 CT Surg Pts adults and peds (China)	To investigate the relationship between length of	16.4% (95% CI: 12.3-21.2) Peds 4.3%, Adults 18.8%	Age, Disease Category, Corticosteroids ($p<0.05$).	Time on CPB not sig. Sex, weight, introp vasoactive and post op vasoactive agents not sig.

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			OR ICU	surgery and incidence of PI in cardiovascular surgical patients.			Length of Surgery sig diff between group with/without PI (p=0.03).
Borghardt, et al, 2015	Prospective Cohort Study	III B	77 patients from mixed ICU population (Brazil). ICU Mixed	Identify the incidence of PI and describe the factors associated with its development in adults hospitalized in ICU.	17 PI 22% (95% CI: 12.6, 31.5)	Sig values in bivariate analysis LOS>10 days (P-.000) CHF Yes: (P-.008) Death: (p-0.001) Braden Risk <11 (p.003)	5 CHF pts/4 developed PI 59% of PI positive pts died
Kang & Zhai, 2015	Meta-analysis of Surgical Patient PI risk and DM	I A (? Level of sig less since no RCT in analysis?)	13 Studies with 2367 patients and 12053 controls. Surgery types; Cardiac (4), General (5), Hip Fracture	To assess diabetes as a risk factor for PI in patients undergoing different types of surgery.	Pooled OR 1.74 (95%CI= 1.40-2.15, I^2=51.1%) Cardiac Studies:	OR of PI in DM patients significant in all 4 Cardiac Surgery Studies What was the OR	Restricted movement from cardiac assist devices (balloon pump, LVAD, and heart failure) considered to be contributing factors No increased PI incidence observed

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			(2), LE Amp (2)		OR=2.0, 95%CI=1.42-2.82, I^2= 0%;		in pts undergoing Hip Surgery
Cox & Roche 2015	Retrospective correlational	III A	306 Patients 2 ICUs Medical-Surgical and Cardiac Surgery ICU	Examine associations between type, dose and duration of administration of vasopressor agents of PI in ICU patients in medical-surgical and CT surgery units and examine factor significantly predictive of development of PI.	13% (41/306)	39% of PI DTI; 56% sacrum 84% (257/306) Received norepinephrine. 37/41 (90% norepinephrine) Log regression predictors: 1. Arrest (B=1.359, p=0.05 OR 3.894, CI=0.998-15.118), 2. Mechanical ventilation longer than 72 hours (B=3.161; P<.001; OR=23.604,	Pts with PI had sig longer infusion times of vasopressin (32 vs 87 hours; p=0.005) longer infusion times of high dose vasopressin (20 vs. 57 hours, p=0.03). Pts receiving 2 pressors significant in PI pts (norepi and vasopressin (X^2=39.3, p<0.001) Longer infusion times at a dose at 0.03 U/min or higher may be "tipping point" for PI development.

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						95%CI 6.427-86.668 3. Hours MAP less than 60mmhg while on pressor (B=0.092; P=0.01; OR=1.096; 95%CI= 1.020-1.178 4. Admin Vasopressin (B=1.572, P=0.004; OR 4.816; 95% CI 1.666-13.925 5. Cardiac diagnosis at ICU admission (B=-3.360, P=0.03; OR 0.035; 95%CI=0.002-0.764.	
Rao et al, 2016	Systematic Review	III A	12 Studies Mixed Population: Critical Care,	Identify risk factors associated with PI development among	Not reported	**PREOP RISKS** SCI (OR 16.8) HX PI (OR 13.51)	Noted absence of DTI discussion in the research for Cardiac Surgery Patients.

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			Surgical ICU or Cardiac Surgery Populations OR/ICU Studies	critically ill, adult, cardiac surgery patients.		Skin prob in Pu areas (OR 4.7) HD 24hrs (OR 4.77) HD 48 hrs. (OR 9.43) Creatinine >3 mg/dl (OR 3.70) Limited Mobility (OR 2.27 and 4.42 based on 2 studies) Fecal INC (OR 3.27) Age (OR 1.03, 2.9, 5.38 in 3 studies) Vascular Disease (OR 2.95, 4.51, 1.80 in 3 studies) Anemia (OR 2.81) Severity of Illness (OR 2.49, 3.40, 2.32 in 3 studies). DM (OR 2.70, 1.85, 1.49 in 4 studies) Malnut (OR 1.61) Malig Tumor (OR 1.48)	Suggest "hypoxic-reperfusion" is linked to DTI and has not been adequately represented in the theoretical framework of PI development.

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						Pain (OR 1.43) Gen Skin problem (OR 1.34) Low Preop Braden (OR 1.22, 1.21 in 2 studies) Low wt/BMI (OR 1.01, 1.03 in 2 studies) Admit Hgb (no OR listed) **INTRAOP** Friction/shear (OR 5.72, 1.72 in 2 studies) LOS > 3day (OR 2.76) Total # surgeries (OR 2.23) Total time in OR (OR 1.07) Hours in ICU (OR 1.01) **POSTOP**	

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						Vasopressor (OR 1.02, 6.05, 8.11, 1.33 in 4 studies) Mech Vent (OR 4.82) Sedative drug (OR 1.61) Post op Steroids and Post op Braden (No OR listed).	
Robich, et al 2017	Retrospective	III A	N=588,417; n=4377 Never Events OR/ICU	Evaluated the nature, risk factors, and outcomes of never events following CABG, valve repair or replacement or thoracic aneurysm repair.	4% PI Stage ¾ over 8-year range (0% 2003-2007) (12% 2008-2011)	Risk factors reported for all possible never events. Pressure ulcers not reported individually. Never events significant for higher Mortality, LOS, Hospital Cost.	Sig risk factors of all never events matching previously reported PI risks: (weight loss, cancer, diabetes, CHF, Gender, Ethnicity, HTN, Age,) Coagulopathy)These were significant in bivariate and the first column in multivariate

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Lu, et al 2017	Prospective Consecutive Cohort	III A	149 Patients (China) OR/ICU	To build a new nomogram score and test its calibration and discrimination power for predicting surgical PI in cardiovascular surgical patients.	24.8% (94% CI 18.1-32.6)	Sig level of <.10 for Log Reg model: Valvular Disease (p=0.063) CAD p<0.03; Wt (p< 0.091), Surgery duration p<0.036; Corticosteroids (p < ; OR for these factors?	94.6% Stage 1 PI, Rest Stg 2. Not significant: gender, wt, alb level, smoke status, DM, CPB duration, post op mech vent duration, vasoactive agents intra or post op were not different between PI/No PI (p>.10). Authors developed predictive nomogram with significant goodness of fit where by pts with probability scores greater than 0.25 should be considered high risk.
Kirkland-Kyhn, et al 2017	5-year Retrospective Descriptive	III B	119 patients (US) 7 ICUs (cardiac surgery, trauma surgery, burn surgery, med-	Identify common patient characteristics and factors that contribute to development	47 HAPU, 72 non-PU	Dialysis OR 4.0 (95%CI--.06-0.99, p=0.05) Shock state (yes/no) OR 10.0 (95%CI 0.025-0.43, p=0.002)	For every hour in surgery odds of DTI increased by 20%

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			surgery, neurosurgery, medical, transfer ICU	of DTIs that evolved into stage 3, stage 3 and unstageable HAPU in ICU patients. Secondary purpose to define specific parameters for risk factors to identify patients at risk for HAPU within ICU Population.		DBP OR 0.93 (95%CI 0.88-0.99, p=0.02) Time surgery in Hours OR 1.20 (95% 1.07-1.33, p=0.001).	

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Key to abbreviations in the table: ALB-albumin; CAD-Coronary artery disease; CPB-cardiopulmonary bypass; DBP-diastolic blood pressure; DM-diabetes mellitus; CT surg-cardiothoracic surgery; HAPU-Hospital acquired pressure ulcer; Hgb- Hemoglobin; HCT-hematocrit; HD-Hemodialysis; HTN-hypertension; ICU-Intensive Care Unit; INC-incontinence; intraop-intraoperative; LOS-Length of stay; OR-operating room; POD-Post operative day; SBP-systolic blood pressure; SCI-spinal cord injury; wt.-Weight

TABLE 3: Common Risk Factors of All Included Studies

MOST COMMON PREDICTORS IN STUDIES WITH MULTIVARIATE ANALYSIS											
ARTICLE	ASA Score	Age	DM	SBP <80, DBP<60	Arrest/MI	Cortico-steroids	Low BMI	OR TIME	Cardiac Dx/Dz Cat	Braden	Mech Vent
Li, et al, 2008			√								
Primiano, et al, 2011	√										
Ghavidel et al, 2012		√	√	√	√						
Liu, He & Chen, 2012			√								
O'Brien, et al 2013	√					√	√		√		√
Shen, et al 2015		√						√			
Borghardt, et al 2015									√	√	
Kang & Zhai, 2015			√								
Cox & Roche, 2015				√	√	√			√		√
Rao, et al 2016*	√		√			√	√	√		√	√
Lu, et al, 2017							√	√	√		
Kirkland-Kyhn, et al 2017				√	√			√			
Robich, et al 2017		√				√	√		√		
Chen et al 2018		√						√	√		

*Systematic Review

Abbreviations: ASA-Anesthesia Severity Assessment; DM-Diabetes Mellitus; SBP-Systolic Blood Pressure; DBP-Diastolic Blood Pressure; MI-Myocardial infarction; BMI-Basal Metabolic Index; OR-Operating Room; Dx-Diagnosis; Dz-Disease; Mech Vent-Mechanical Ventilation

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Conceptual Framework

Conceptual Framework of Pressure Injury Development in Cardiac Surgery Patients

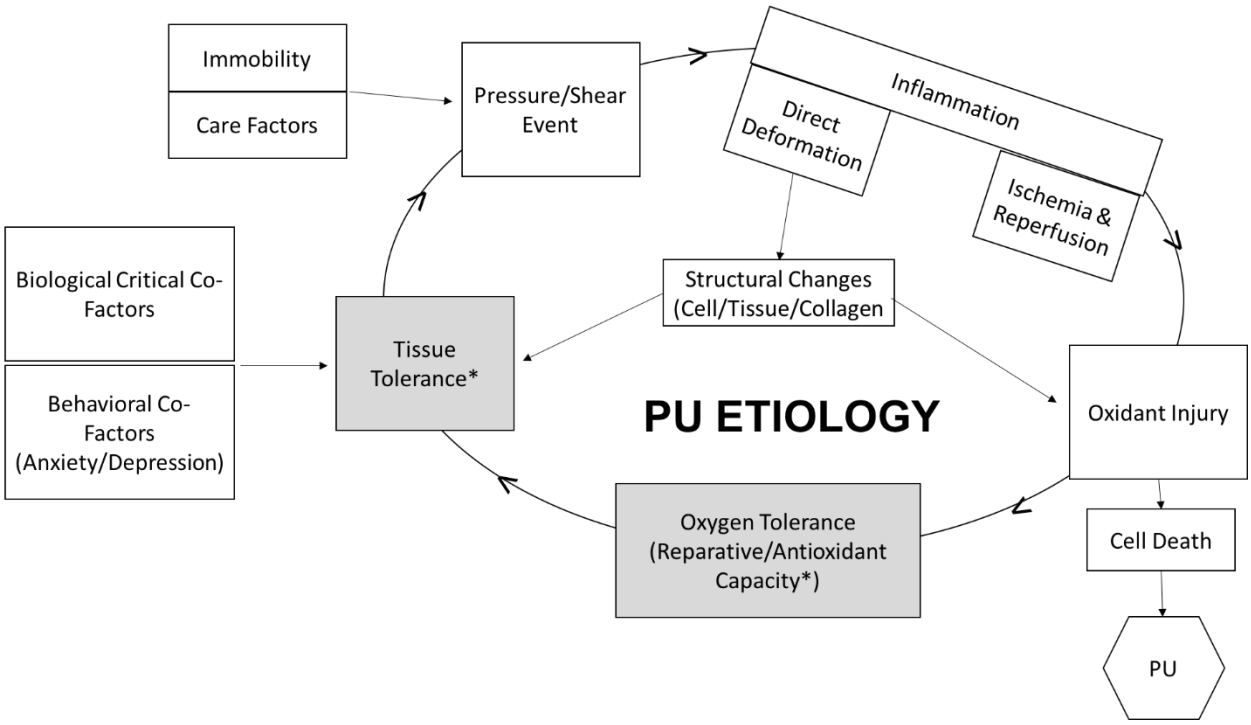

Figure 4. As described below, the theoretical development of pressure injuries in the cardiac surgery patient from baseline biobehavioral risk factors and influence of immobility and care factors on the cumulative and repetitive process of oxidant injury following a pressure and shear event. Ultimately, repetitive injury leads to pressure injury when there is imbalance between oxidant injury and reparative mechanisms. Oxidant injury may be exacerbated by baseline biobehavioral risk factors, which alter host inflammatory response, such as anxiety and depression. * Denotes protective mechanism.

Description of Conceptual Framework

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Given the complexities of PI etiology and the relative unknowns that remain, I seek an estimation of the truth, and therefore will utilize the philosophical perspective of post-positivism (Creswell, 2013). The four assumptions associated with this perspective are as follows: 1.) An ontological belief that there is only one reality separate from and incapable of being understood by all; 2) Epistemologic position that robust research principles and statistics may be utilized to approximate the truth about reality, yet absolute truth will never be truly known; 3.) The axiological understanding that as the researcher, personal biases cannot be introduced into the research and limited interaction with the subjects is important; and 4.) Methodological importance of scientific inquiry with a goal to create new knowledge. Post-positivism is appropriate as the complexity of PI etiology will require multiple theories, methods, and approaches to seek new understanding of their development.

Post-positivist philosophical assumptions inform the theoretical framework for the study of patient factors, behavioral conditions, biochemical pathophysiological pathways, and the role of the care factors in PI development. Thus, the framework reflects the post-positivist assumption that knowledge can be created by studying both observable and unobservable phenomena. This framework was also developed through adaptation of prior conceptual models and evidence in the literature describing the links between critical cofactors, subsequent host tissue tolerance and PI risk (Bhargava, Chanmugam, & Herman, 2014; Braden & Bergstrom, 1987; Coleman et al., 2014; Defloor, 1999; Claudia Gorecki et al., 2010). However, unique to this framework is the inclusion of the cumulative impact of repetitive pressure and shear events on progressive, uncontrolled oxidant injury. This is particularly important because prior research was based on the conceptualization of PI development in relation to a single pressure/shear event. Yet, surgical patients sustain repeated injury through routine care and transitions of care

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including in the emergency department, following prolonged time on the operating table, in the ICU, and during diagnostic procedures. Repeated instances of immobility and pressure/shear events necessitate consideration of ongoing and progressive injury potential. Thus, for the VAD-TAH patient, these events occur from the pre-surgical suite, through operating room procedures and during immediate post-operative care in the ICU. Additionally, patients present with variable biobehavioral factors that influence response to these pre-intra-post-operative immobility and pressure/shear events.

The conceptual framework is an overarching framework of the development of PI in the cardiac surgery patient, considering the cyclical complexity of PI development, including baseline biobehavioral risk factors, the care setting, and the biochemical response of injured tissue.

Preoperative Risk and Baseline Tissue Tolerance

Baseline demographic and biobehavioral cofactors (sex, age, race, type 1 and type 2 diabetes, smoking, anxiety and depression) influence the patient's tissue tolerance, namely, their ability to respond to inflammatory and structural damage following pressure/shear events. There are conflicting results as to whether sex is a predictor of PI development, however; heart disease disproportionately effects women and is the leading cause of death, with risk factors similar to that of PI (Bergstrom, Braden, Kemp, Champagne, & Ruby, 1996; Lindgren et al., 2005; Xu, Murphy, Kochanek, & Bastian, 2016).

Age is associated with a higher risk for PI development in multiple studies of cardiac surgery patients and is associated with risk during operative procedures (Chen, Shen, Xu, Zhang, & Wu, 2015; Cox, 2011, 2011; Feuchtinger et al., 2005; Halfens, Van Achterberg, & Bal, 2000;

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Lindgren, Unosson, Fredrikson, & Ek, 2004; Lumbley, Ali, & Tchokouani, 2014; Manzano et al., 2010; O'Brien et al., 2014; Papantonio, Wallop, & Kolodner, 1994; Perneger et al., 2002; Sewchuk, Padula, & Osborne, 2006; Slowikowski & Funk, 2010; Webster et al., 2011). African American race was found to be a predictor of PI in acute care hospitals (Fogerty et al., 2008) and African Americans were at higher risk than Caucasians in all age groups in another study (Fogerty, Guy, Barbul, Nanney, & Abumrad, 2009). Regarding diabetes mellitus (DM), a meta-analysis of 2453 patients found that DM was significantly associated with PI ($p < .00001$) and the only independent risk factor for PI (Liu, He, & Chen, 2012), while intraoperatively, surgical patients with DM were 49% more likely to develop PI (Tschannen, Bates, Talsma, & Guo, 2012). Smoking may impact the inflammatory and oxidative response following tissue injury, impair perfusion to the site and overall tissue oxygenation. Smoking was identified as a risk factor for PI development and has been included in risk assessment instruments (Suriadi et al., 2007; Suriadi, Sanada, Sugama, Thigpen, & Subuh, 2008).

The influence of care factors reflects the role of the provider, engagement of the patient and the preventive equipment for mitigating PI risk, such as: turning and repositioning, specialty beds/surfaces, and patient education and understanding of risk, (Bergstrom et al., 2013; McInnes et al., 2015; Stone et al., 2015). These factors are reliably controlled at the proposed setting of research using setting specific PI prevention protocols that are the standard of care for intraoperative and postoperative settings, are integrated into the electronic health record, and are individualized to the patients based on subscale-scores of the Braden Risk Assessment Scale score, which directs escalating preventive interventions.

Depression and anxiety are identified as cofactors in the framework because they are prevalent conditions in the VAD-TAH population (17% and 42% respectively) (Huffman,

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Celano, & Januzzi, 2010) compared to non-device cardiac counterparts (Estep et al., 2015; Reynard, Butler, McKee, Starling, & Gorodeski, 2014; Shapiro, Levin, & Oz, 1996; Snipelisky et al., 2015). Additionally, depression and anxiety are suggested to be associated with increased PI risk (Braden, 1998; Krause & Broderick, 2004; Krueger, Noonan, Williams, Trenaman, & Rivers, 2013) related to increased production of inflammatory cytokines, catecholamines, and corticosteroids by activation of the Hypothalamus-Pituitary-Axis and Sympathetic Medullary Axis, which is thought to increase risk of post-operative complications in cardiac patients (Doering, Moser, Lemankiewicz, Luper, & Khan, 2005). Thus, levels of depression and anxiety biologically contribute to PI risk in cardiac surgery patients through the following mechanisms: 1.) Exacerbating the response to cellular damage and inflammation resulting from ischemia; 2.) Exacerbating control of subsequent re-injury during reperfusion which causes oxidative stress, DNA damage and apoptosis in the skeletal muscle; 3.) Alteration of systemic and cellular temperature exacerbating both ischemia and inflammation (Bhargava et al., 2014); and 4.) Care factors such as adherence to rehabilitation plans (turning, walking, repositioning) thereby increasing immobility time (Shapiro et al., 1996). Subsequently, depression and anxiety are linked to tissue tolerance, oxidant tolerance and the pressure/shear event itself as depicted in the conceptual model.

Next, the framework describes the cumulative nature of PI etiology. Pressure and shear events trigger inflammation, leading to decreased oxygen delivery to the muscle tissue, anaerobic respiration and the development of oxidant injury during ischemia. This ischemic injury is then exacerbated when blood supply is returned (reperfusion) after repositioning the patient, leading to a secondary injury, reperfusion injury. Reperfusion is described as a complex mixture of biochemical inflammatory cascades that exacerbate ischemic injury, with both systemic and local

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inflammatory response (Duehrkop & Rieben, 2014). Skeletal muscle (where PI injury starts) is more susceptible to ischemia than skin, bone or nerves due to its higher metabolic demand for oxygen (Berlowitz & Brienza, 2007; Wilson et al., 2015). Most muscle cell death occurs during the reperfusion phase and may progress after resolution of ischemia due to the response of the innate immune system propagating reactive oxygen species (ROS) production and subsequent lipid peroxidation (Kirisci et al., 2013; Wilson et al., 2015). The severity of reperfusion is determined by the time of ischemia, which is the amount of time the tissues are deprived of oxygen (Gefen et al., 2008; Leopold & Gefen, 2012). The best estimation of IR is immobility time and the risk for PI can be operationalized in the cardiac surgery patient by evaluating total time immobilized from perioperative unit through intensive care unit arrival, anesthesia time, and cardiopulmonary bypass time. There is a *cumulative impact* of oxidant stressors, with injury recovery versus injury progression dependent on the patient's capacity to generate antioxidant, anti-complement, and an appropriately regulated innate immune response. Thus, damage to the tissues may continue following a single reperfusion event and be compounded when additional pressure and shear events occur, leading to further oxidant induced injury.

Therefore, oxidative stress may be conceptualized as the individual's *tissue tolerance to oxygen* (Rao et al., 2016). The amount of oxidant injury can be measured by levels of circulating F_2-Isoprostane and corresponding urinary metabolites of 2,3, dinor-15- F_2-Isoprostane and 5,6,dihydro-15- F_2-Isoprostane, which are established markers of oxidative stress (Milne, Dai, & Roberts, 2015; Morrow, Awad, Kato, et al., 1992; Morrow et al., 1990; Morrow, Awad, Boss, Blair, & Roberts, 1992). These markers are by-products of the arachidonic acid pathway expressed following excessive ROS production during hypoperfusion and IR, leading to lipid peroxidation of polyunsaturated fatty acids in the phospholipid bilayer of cell membranes (Milne

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et al., 2015; Repetto et al., 2012). In summary, a cumulative cycle of oxidative stress develops following decreased perfusion, oxygenation and subsequent reperfusion after each pressure and shear event. Ultimately, oxidant injury alters tissue tolerance and leads to cell death and PI formation.

Summary of Philosophy and Conceptual Framework

Given the complexity of PI pathophysiology, it is recognized that gaining an absolute understanding of every pathologic mechanism is not possible. Additionally, a post-positivist paradigm emphasizes the fact that while all measurement is fallible, unobservable phenomena have existence and inform observable effects. Therefore, multiple measures, theories or data sources may be required to examine a phenomena utilizing strict adherence to well-designed methodological approaches to decrease bias and improve the probabilistic approximation of the truth (Houghton, Hunter, & Meskell, 2012).

Bergstrom, N., Braden, B., Kemp, M., Champagne, M., & Ruby, E. (1996). Multi-site study of incidence of pressure ulcers and the relationship between risk level, demographic characteristics, diagnoses, and prescription of preventive interventions. *Journal of the American Geriatrics Society*, *44*, 22–30.

Bergstrom, N., Horn, S. D., Rapp, M. P., Stern, A., Barrett, R., & Watkiss, M. (2013). Turning for Ulcer Reduction: a multisite randomized clinical trial in nursing homes. *Journal of the American Geriatrics Society*, *61*, 1705–1713. https://doi.org/10.1111/jgs.12440

Berlowitz, D. R., & Brienza, D. M. (2007). Are all pressure ulcers the result of deep tissue injury? A review of the literature. *Ostomy/Wound Management*, *53*, 34–38.

Bhargava, A., Chanmugam, A., & Herman, C. (2014). Heat transfer model for deep tissue injury: a step towards an early thermographic diagnostic capability. *Diagnostic Pathology*, *9*, 36. https://doi.org/10.1186/1746-1596-9-36

www.manaraa.com

Braden, B., & Bergstrom, N. (1987). A conceptual schema for the study of the etiology of pressure sores. *Rehabilitation Nursing: The Official Journal of the Association of Rehabilitation Nurses*, *12*, 8–12.

Braden, B. J. (1998). The relationship between stress and pressure sore formation. *Ostomy/Wound Management*, *44*(3A Suppl), 26S–36S; discussion 37S.

Chen, H.-L., Shen, W.-Q., Xu, Y.-H., Zhang, Q., & Wu, J. (2015). Perioperative corticosteroids administration as a risk factor for pressure ulcers in cardiovascular surgical patients: a retrospective study. *International Wound Journal*, *12*, 581–585. https://doi.org/10.1111/iwj.12168

Coleman, S., Gorecki, C., Nelson, E. A., Closs, S. J., Defloor, T., Halfens, R., … Nixon, J. (2013). Patient risk factors for pressure ulcer development: systematic review. *International Journal of Nursing Studies*, *50*, 974–1003. https://doi.org/10.1016/j.ijnurstu.2012.11.019

Coleman, S., Nixon, J., Keen, J., Wilson, L., McGinnis, E., Dealey, C., … Nelson, E. A. (2014). A new pressure ulcer conceptual framework. *Journal of Advanced Nursing*, *70*(10), 2222–2234. https://doi.org/10.1111/jan.12405

Cox, J. (2011). Predictors of pressure ulcers in adult critical care patients. *American Journal of Critical Care: An Official Publication, American Association of Critical-Care Nurses*, *20*, 364–375. https://doi.org/10.4037/ajcc2011934

Defloor, T. (1999). The risk of pressure sores: a conceptual scheme. *Journal of Clinical Nursing*, *8*, 206–216.

Doering, L. V., Moser, D. K., Lemankiewicz, W., Luper, C., & Khan, S. (2005). Depression, healing, and recovery from coronary artery bypass surgery. *American Journal of Critical Care: An Official Publication, American Association of Critical-Care Nurses*, *14*, 316–324.

Duehrkop, C., & Rieben, R. (2014). Refinement of tourniquet-induced peripheral ischemia/reperfusion injury in rats: comparison of 2 h vs 24 h reperfusion. *Laboratory Animals*, *48*, 143–154. https://doi.org/10.1177/0023677213516313

Estep, J. D., Starling, R. C., Horstmanshof, D. A., Milano, C. A., Selzman, C. H., Shah, K. B., … ROADMAP Study Investigators. (2015). Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients: Results from the ROADMAP Study. *Journal of the American College of Cardiology*, *66*, 1747–1761. https://doi.org/10.1016/j.jacc.2015.07.075

Feuchtinger, J., Halfens, R., & Dassen, T. (2007). Pressure ulcer risk assessment immediately after cardiac surgery--does it make a difference? A comparison of three pressure ulcer risk assessment instruments within a cardiac surgery population. *Nursing in Critical Care*, *12*, 42–49. https://doi.org/10.1111/j.1478-5153.2006.00198.x

www.manaraa.com

Feuchtinger, J., Halfens, R. J. G., & Dassen, T. (2005). Pressure ulcer risk factors in cardiac surgery: a review of the research literature. *Heart & Lung: The Journal of Critical Care*, *34*, 375–385. https://doi.org/10.1016/j.hrtlng.2005.04.004

Fogerty, M. D., Abumrad, N. N., Nanney, L., Arbogast, P. G., Poulose, B., & Barbul, A. (2008). Risk factors for pressure ulcers in acute care hospitals. *Wound Repair and Regeneration: Official Publication of the Wound Healing Society [and] the European Tissue Repair Society*, *16*, 11–18. https://doi.org/10.1111/j.1524-475X.2007.00327.x

Fogerty, M., Guy, J., Barbul, A., Nanney, L. B., & Abumrad, N. N. (2009). African Americans show increased risk for pressure ulcers: a retrospective analysis of acute care hospitals in America. *Wound Repair and Regeneration: Official Publication of the Wound Healing Society [and] the European Tissue Repair Society*, *17*, 678–684. https://doi.org/10.1111/j.1524-475X.2009.00522.x

Gefen, A., van Nierop, B., Bader, D. L., & Oomens, C. W. (2008). Strain-time cell-death threshold for skeletal muscle in a tissue-engineered model system for deep tissue injury. *Journal of Biomechanics*, *41*, 2003–2012. https://doi.org/10.1016/j.jbiomech.2008.03.039

Gorecki, C., Lamping, D. L., Brown, J. M., Madill, A., Firth, J., & Nixon, J. (2010). Development of a conceptual framework of health-related quality of life in pressure ulcers: a patient-focused approach. *International Journal of Nursing Studies*, *47*, 1525–1534. https://doi.org/10.1016/j.ijnurstu.2010.05.014

Halfens, R. J., Van Achterberg, T., & Bal, R. M. (2000). Validity and reliability of the Braden scale and the influence of other risk factors: a multi-centre prospective study. *International Journal of Nursing Studies*, *37*, 313–319.

Huffman, J. C., Celano, C. M., & Januzzi, J. L. (2010). The relationship between depression, anxiety, and cardiovascular outcomes in patients with acute coronary syndromes. *Neuropsychiatric Disease and Treatment*, *6*, 123–136.

Kirisci, M., Oktar, G. L., Ozogul, C., Oyar, E. O., Akyol, S. N., Demirtas, C. Y., & Arslan, M. (2013). Effects of adrenomedullin and vascular endothelial growth factor on ischemia/reperfusion injury in skeletal muscle in rats. *The Journal of Surgical Research*, *185*, 56–63. https://doi.org/10.1016/j.jss.2013.05.053

Krause, J. S., & Broderick, L. (2004). Patterns of recurrent pressure ulcers after spinal cord injury: identification of risk and protective factors 5 or more years after onset. *Archives of Physical Medicine and Rehabilitation*, *85*, 1257–1264. https://doi.org/10.1016/j.apmr.2003.08.108

Krueger, H., Noonan, V. K., Williams, D., Trenaman, L. M., & Rivers, C. S. (2013). The influence of depression on physical complications in spinal cord injury: behavioral mechanisms and health-care implications. *Spinal Cord*, *51*, 260–266. https://doi.org/10.1038/sc.2013.3

www.manaraa.com

Leopold, E., & Gefen, A. (2012). A simple stochastic model to explain the sigmoid nature of the strain-time cellular tolerance curve. *Journal of Tissue Viability*, *21*, 27–36. https://doi.org/10.1016/j.jtv.2011.11.002

Lindgren, M., Unosson, M., Fredrikson, M., & Ek, A.-C. (2004). Immobility--a major risk factor for development of pressure ulcers among adult hospitalized patients: a prospective study. *Scandinavian Journal of Caring Sciences*, *18*, 57–64.

Lindgren, M., Unosson, M., Krantz, A.-M., & Ek, A.-C. (2005). Pressure ulcer risk factors in patients undergoing surgery. *Journal of Advanced Nursing*, *50*, 605–612. https://doi.org/10.1111/j.1365-2648.2005.03441.x

Liu, P., He, W., & Chen, H.-L. (2012). Diabetes mellitus as a risk factor for surgery-related pressure ulcers: a meta-analysis. *Journal of Wound, Ostomy, and Continence Nursing: Official Publication of The Wound, Ostomy and Continence Nurses Society / WOCN*, *39*, 495–499. https://doi.org/10.1097/WON.0b013e318265222a

Lumbley, J. L., Ali, S. A., & Tchokouani, L. S. (2014). Retrospective review of predisposing factors for intraoperative pressure ulcer development. *Journal of Clinical Anesthesia*, *26*, 368–374. https://doi.org/10.1016/j.jclinane.2014.01.012

Manzano, F., Navarro, M. J., Roldan, D., Moral, M. A., Leyva, I., Guerrero, C., … Fernandez-Mondejar, E. (2010). Pressure ulcer incidence and risk factors in ventilated intensive care patients. *Journal of Critical Care*, *25*, 469–476. https://doi.org/10.1016/j.jcrc.2009.09.002

McInnes, E., Jammali-Blasi, A., Bell-Syer, S. E. M., Dumville, J. C., Middleton, V., & Cullum, N. (2015). Support surfaces for pressure ulcer prevention. *The Cochrane Database of Systematic Reviews*, *9*, CD001735. https://doi.org/10.1002/14651858.CD001735.pub5

Milne, G. L., Dai, Q., & Roberts, L. J. (2015). The isoprostanes--25 years later. *Biochimica Et Biophysica Acta*, *1851*, 433–445. https://doi.org/10.1016/j.bbalip.2014.10.007

Milne, G. L., Gao, B., Terry, E. S., Zackert, W. E., & Sanchez, S. C. (2013). Measurement of F2-isoprostanes and isofurans using gas chromatography-mass spectrometry. *Free Radical Biology & Medicine*, *59*, 36–44. https://doi.org/10.1016/j.freeradbiomed.2012.09.030

Morrow, J. D., Awad, J. A., Boss, H. J., Blair, I. A., & Roberts, L. J. (1992). Non-cyclooxygenase-derived prostanoids (F2-isoprostanes) are formed in situ on phospholipids. *Proceedings of the National Academy of Sciences of the United States of America*, *89*, 10721–10725.

Morrow, J. D., Awad, J. A., Kato, T., Takahashi, K., Badr, K. F., Roberts, L. J., & Burk, R. F. (1992). Formation of novel non-cyclooxygenase-derived prostanoids (F2-isoprostanes) in carbon tetrachloride hepatotoxicity. An animal model of lipid peroxidation. *The Journal of Clinical Investigation*, *90*, 2502–2507. https://doi.org/10.1172/JCI116143

Morrow, J. D., Hill, K. E., Burk, R. F., Nammour, T. M., Badr, K. F., & Roberts, L. J. (1990). A series of prostaglandin F2-like compounds are produced in vivo in humans by a non-

www.manaraa.com

cyclooxygenase, free radical-catalyzed mechanism. *Proceedings of the National Academy of Sciences of the United States of America*, *87*, 9383–9387.

O'Brien, D. D., Shanks, A. M., Talsma, A., Brenner, P. S., & Ramachandran, S. K. (2014). Intraoperative risk factors associated with postoperative pressure ulcers in critically ill patients: a retrospective observational study. *Critical Care Medicine*, *42*, 40–47. https://doi.org/10.1097/CCM.0b013e318298a849

Papantonio, C. T., Wallop, J. M., & Kolodner, K. B. (1994). Sacral ulcers following cardiac surgery: incidence and risks. *Advances in Wound Care: The Journal for Prevention and Healing*, *7*, 24–36.

Perneger, T. V., Raë, A. C., Gaspoz, J. M., Borst, F., Vitek, O., & Héliot, C. (2002). Screening for pressure ulcer risk in an acute care hospital: development of a brief bedside scale. *Journal of Clinical Epidemiology*, *55*, 498–504.

Rao, A. D., Preston, A. M., Strauss, R., Stamm, R., & Zalman, D. C. (2016). Risk Factors Associated With Pressure Ulcer Formation in Critically Ill Cardiac Surgery Patients: A Systematic Review. *Journal of Wound, Ostomy, and Continence Nursing*, *43*, 242–247. https://doi.org/10.1097/WON.0000000000000224

Repetto, M., Semprine, J., & Boveris, A. (2012). Lipid Peroxidation: Chemical Mechanism, Biological Implications and Analytical Determination. In A. Catala (Ed.), *Lipid Peroxidation*. Retrieved from http://www.intechopen.com/books/lipid-peroxidation/lipid-peroxidation-chemical-mechanism-biological-implications-and-analytical-determination

Reynard, A. K., Butler, R. S., McKee, M. G., Starling, R. C., & Gorodeski, E. Z. (2014). Frequency of depression and anxiety before and after insertion of a continuous flow left ventricular assist device. *The American Journal of Cardiology*, *114*, 433–440. https://doi.org/10.1016/j.amjcard.2014.05.015

Sewchuk, D., Padula, C., & Osborne, E. (2006). Prevention and early detection of pressure ulcers in patients undergoing cardiac surgery. *AORN Journal*, *84*, 75–96.

Shapiro, P. A., Levin, H. R., & Oz, M. C. (1996). Left ventricular assist devices. Psychosocial burden and implications for heart transplant programs. *General Hospital Psychiatry*, *18*(6 Suppl), 30S–35S.

Slowikowski, G. C., & Funk, M. (2010). Factors associated with pressure ulcers in patients in a surgical intensive care unit. *Journal of Wound, Ostomy, and Continence Nursing*, *37*, 619–626. https://doi.org/10.1097/WON.0b013e3181f90a34

Snipelisky, D., Stulak, J. M., Schettle, S. D., Sharma, S., Kushwaha, S. S., & Dunlay, S. M. (2015). Psychosocial characteristics and outcomes in patients with left ventricular assist device implanted as destination therapy. *American Heart Journal*, *170*, 887–894. https://doi.org/10.1016/j.ahj.2015.08.012

www.manaraa.com

Stone, A., Brienza, D., Call, E., Fontaine, R., Goldberg, M., Hong, K. Z., … Sylvia, C. (2015). Standardizing Support Surface Testing and Reporting: A National Pressure Ulcer Advisory Panel Executive Summary. *Journal of Wound, Ostomy, and Continence Nursing*, *42*, 445–449. https://doi.org/10.1097/WON.0000000000000172

Suriadi, null, Sanada, H., Sugama, J., Thigpen, B., & Subuh, M. (2008). Development of a new risk assessment scale for predicting pressure ulcers in an intensive care unit. *Nursing in Critical Care*, *13*, 34–43. https://doi.org/10.1111/j.1478-5153.2007.00250.x

Suriadi, Sanada, H., Sugama, J., Kitagawa, A., Thigpen, B., Kinosita, S., & Murayama, S. (2007). Risk factors in the development of pressure ulcers in an intensive care unit in Pontianak, Indonesia. *International Wound Journal*, *4*, 208–215. https://doi.org/10.1111/j.1742-481X.2007.00315.x

Tschannen, D., Bates, O., Talsma, A., & Guo, Y. (2012). Patient-specific and surgical characteristics in the development of pressure ulcers. *American Journal of Critical Care: An Official Publication, American Association of Critical-Care Nurses*, *21*, 116–125. https://doi.org/10.4037/ajcc2012716

Webster, J., Coleman, K., Mudge, A., Marquart, L., Gardner, G., Stankiewicz, M., … McClymont, A. (2011). Pressure ulcers: effectiveness of risk-assessment tools. A randomised controlled trial (the ULCER trial). *BMJ Quality & Safety*, *20*, 297–306. https://doi.org/10.1136/bmjqs.2010.043109

Wilson, H.-M. P., Welikson, R. E., Luo, J., Kean, T. J., Cao, B., Dennis, J. E., & Allen, M. D. (2015). Can Cytoprotective Cobalt Protoporphyrin Protect Skeletal Muscle and Muscle-derived Stem Cells From Ischemic Injury? *Clinical Orthopaedics and Related Research*, *473*, 2908–2919. https://doi.org/10.1007/s11999-015-4332-8

Xu, J., Murphy, S. L., Kochanek, K. D., & Bastian, B. A. (2016). Deaths: Final Data for 2013. *National Vital Statistics Reports: From the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System*, *64*, 1–119.

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Manuscript 2

Incidence and Predictor Variables of Pressure Injuries in Patients Undergoing Ventricular Assist Device and Total Artificial Heart Surgeries: An Eight-Year Retrospective Review

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ABSTRACT

BACKGROUND

Cardiac surgery patients undergoing on-pump cardiac surgery have some of the highest reported incidence and prevalence of pressure injuries (PI). A growing subset of cardiac surgery include patients with end-stage heart failure who undergo ventricular assist device (VAD) or total artificial heart (TAH) surgery. The specific risk factors for PI development remain unexplored.

PURPOSE

The aim of this dissertation research is to investigate the incidence and risk factors associated with PI development in patients undergoing VAD-TAH surgery, which will inform an overall developing program of research in PI etiology, risk reduction, and prevention in this high-risk population. A full understanding of PI etiology is the foundation for risk reduction and prevention.

METHODS

A retrospective study of all VAD-TAH surgeries between 2010-2018 was performed in a designated heart center at a large academic health system. The study evaluated the incidence of pressure ulcers by case, patient and incidence density for each of the respective 1000 patient days during the study period. Univariate statistics are reported by four different VAD-TAH devices. Variables significant in bivariate analysis were entered in a stepwise logistic regression model.

RESULTS

The final sample for investigation included 292 independent VAD-TAH surgical cases conducted in 265 patients. In total, 32 patients developed 45 pressure ulcers. The incidence of PI per all surgical cases was 11% (32/292), with PI incidence per patient of 12% (32/265). Incidence density was found to be (10/1000) 1% for 2010-2012, (12/1000) 1.2% for 2013-2015, and (10/920) 1.1% for 2016-2018 respectively. Logistic regression revealed significant predictor variables for pressure injury in the VAD-TAH population: age, mechanical ventilation time and preoperative Braden Risk Assessment score. Despite long OR and long total immobility times, the mean time to PI was 23 days after admission and over 14 days after surgery, indicating a low rate of intraoperative and ICU associated PI.

CONCLUSIONS

The overall incidence of pressure injury was much lower than anticipated given historical incidence of PI in non-device cardiac surgery patients. A prospective study to further investigate significant risk factors and identify potential preventive mechanisms that decreased PI incidence in this population is warranted.

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INTRODUCTION

Pressure injuries (PI) are defined as, "a localized damage to the skin and underlying soft tissue usually over a bony prominence or related to a medical or other device. The injury can present as intact skin or an open ulcer and may be painful. The injury occurs because of intense and/or prolonged pressure in combination with shear. The tolerance of soft tissue for pressure and shear may also be affected by microclimate, nutrition, perfusion, co-morbidities and condition of the soft tissue." (Edsberg, Black, Golberg, McNichol, Moore & Sieggreen, 2016). Globally, PI prevalence in all settings and patient ages ranges from 27.3% to 72.5%. (Haesler, 2014; Vangilder, Macfarlane, & Meyer, 2008). In a review of acute care settings, prevalence ranges from 0-49% contingent on the care setting and varies with patient population. It has been estimated that of patients who sustain a PI, over 2.5 million patients subsequently develop (PI) resulting in 60,000 deaths annually in the United States. (The Joint Commission, 2008). In the U.S., PI treatment costs may exceed $26.8 billion dollars annually (Padula & Delarmente, 2019). Over the past two decades, over 100 risk factors have been associated with the development of PI. However, these risk factors and associated prevention measures have not been adequately investigated across various cardiac surgery sub-populations (Ettema, et al., 2014). For example, intraoperative incidence rates in non-device cardiac surgery have been reported as high as 29.5%, (Feuchtinger, Halfens, & Dassen, 2005; Rao, Preston, Strauss, Stamm, & Zalman, 2016). Subsequent prospective cohort studies of subpopulations such as cardiac surgery bypass grafting (CABG), the most commonly studied cardiac surgical intervention, have shown incidence rates as high as 53.4% in the cardiac ICU (Schuurman, Schoonhoven, Keller, & van Ramshorst, 2009) and 49% immediately after cardiac surgical procedures (Feuchtinger et al., 2007). However, the

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specific risk factors for the development of PI in ventricular assist device (VAD) and total artificial heart patients (TAH) remain unexplored (Brindle, 2019,[unpublished data]).

Pressure Injury Etiology

The complexity of PI etiology involves the interplay of many pathophysiological processes; however, all of these processes arise from two primary pathophysiologic concepts: ischemia and direct deformation injury (Oomens, Bader, Loerakker, & Baaijens, 2015). First, ischemia results from prolonged compression of the skin and subcutaneous tissues leading to decreased perfusion, lymphatic impairment, tissue hypoxia and ischemia with subsequent reperfusion injury when blood flow is restored (ischemia-reperfusion or IR). This results in intravascular inflammation, complement activation, response of the innate immune system, oxidative stress through the build-up of metabolic waste products and mitochondrial dysregulation with ultimate activation of apoptosis and necrosis pathways (Gefen, Farid, & Shaywitz, 2013; Kirisci, Oktar, Ozogul, Oyar, Akyol, Dermirtas & Arslan, 2013; Puntel, Carvalho, Dobrachinski, Salgueiro & Puntel, 2013; Repetto, Semprine, & Boveris, 2012). Second, direct deformation injury results from the application of pressure and specifically shear forces to the tissues, where cell death is caused by significantly altering cell shape leading to cytoskeletal damage of the cell membrane. Direct deformation injury may cause cell death in the presence of adequate perfusion and oxygenation (Gefen, van Nierop, Bader, & Oomens, 2008; Oomens et al., 2015; Oomens, Loerakker, & Bader, 2010). Therefore, PI may form following prolonged hypoperfusion either related to ischemia and corresponding reperfusion injury or a short duration of intense deformation of the tissues leading to direct cellular injury. These two processes, ischemia and direct deformation, are relevant to the cardiac surgery population because of prolonged periods of immobility experienced on the operating table, compromised

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tissue tolerance and repetitive nature of pressure shear injury and altered systemic inflammatory response to injury

In CABG patients, Feuchtinger and colleagues reported that 47% of PI presented on post-operative day 0, with the remaining 15% developing between day 1 and day 7 after surgery. Additionally, in a study of 135,701 CABG surgeries in the New York state database, patients with mental disorders (schizophrenia, major depression, dementia, bipolar disorder, and other psychiatric conditions) were found to have higher rates of PI than those without mental disorders (7.3/1000 vs. 1.8/1000; AOR 1.42, p=.006) (Li, Glance, Cai, & Mikael, 2008). Specifically, depression and anxiety are suggested to be associated with increased PI risk (Braden, 1998; Krause & Broderick, 2004; Krueger, Noonan, Williams, Trenaman, & Rivers, 2013) related to increased production of inflammatory cytokines, catecholamines, and corticosteroids by activation of the Hypothalamus-Pituitary-Axis and Sympathetic Medullary Axis, which is thought to increase risk of post-operative complications in cardiac patients (Doering, Moser, Lemankiewicz, Luper, & Khan, 2005)..

A systematic review of the literature identified that the most common predictors for cardiac surgery patients after multivariate analysis included: American Society of Anesthesia (ASA) score, age, diabetes, hypotension, cardiac arrest, intravenous corticosteroids, basal metabolic index, surgery time, severity of cardiac disease, Braden Risk Assessment score and mechanical ventilation (Brindle, 2019, [unpublished data]). However, risk factors have not been adequately investigated in patients with purportedly very high risk based on PI etiology and prior research, such as those with advanced heart failure most of whom require surgical intervention

Pressure Injuries in Advanced Heart Failure Patients

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A growing subset of the cardiac surgery patient population includes patients with advancing heart failure (HF) that require implantable ventricular assist devices or a total artificial heart (VAD-TAH). While heart transplantation is a successful treatment for end stage HF patients, it is reported that this is available for less than 10% of patients due to severe shortage of donor organs (Aissaoui, Jouan, Gourjault, Diebold, Ortuno, Hamdan, et al., 2018). In the U.S., the number of persons with HF is anticipated to exceed eight million people by 2030 and is projected to be the leading cause of disability (Silva Enciso, 2016). One retrospective study in patients hospitalized with systolic HF investigated length of stay (LOS), in-hospital mortality and associated predictors. Data was extrapolated from three payer based research databases (Allen, Smoyer Tomic, Wilson, Smith, & Agodoa, 2013). Of the 17,517 patients identified in the study, PI were present in 4% of subjects and increased LOS by 1.36 days ($p<0.0001$) in every payer category (commercial 158/4109; Medicaid 76/2118; Medicare 446/11,370), evidencing a significant patient and economic burden. Due to the high rate of PI in the cardiac surgery population, the impact of VAD-TAH surgery on PI development warrants investigation. While inferences can be made to guide research and patient care, patients undergoing VAD-TAH procedures may differ in risk profile from patients requiring a CABG procedure secondary to: 1) nature and length of the VAD-TAH procedure, 2) prolonged lengths of stay (LOS) associated with VAD-TAH procedures, and 3) abnormal or pulseless blood flow 4) physiological vulnerability and comorbidities of patients with advanced HF.

Given the high prevalence of PI associated with CABG procedure and the additional vulnerability associated with advanced HF and VAD-TAH surgical procedures, it is hypothesized that the VAD-TAH patient is at the highest level of risk for PI development; however, the actual incidence is unknown, representing a large gap in our current understanding

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of PI in this population. With the increasing prevalence of advanced HF and resultant need for high risk VAD-TAH procedures, developing a PI further compounds significant complications that may result in additional physical, psychological and social impacts to patients and a high financial burden for the U.S. healthcare system. Therefore, the aim of this dissertation research is to investigate the incidence and risk factors associated with PI development in patients undergoing VAD-TAH surgery, which will inform an overall developing program of research in PI etiology, risk reduction, and prevention in this high-risk population. A full understanding of PI etiology is the foundation for risk reduction and prevention.

Specific Aims:

The primary aim of this study is to determine the incidence, natural history, and odds of PI development in the VAD-TAH population. The secondary aim is to explore a panel of cofactors as predictor variables in the development of pressure ulcers in the VAD-TAH population. Next, a sub-analysis of the research seeks to compare the association between three immobility times (total immobility time, operating room anesthesia time, cardiopulmonary bypass time) and risk of PI development. Finally, the third aim of this research seeks to explore the biobehavioral relationship between preoperative diagnosis of depression and anxiety, on PI development.

Methods

The design for this study was informed by a systematic review of the literature using PRISMA methodology, which returned zero studies involving PI incidence or risk factors for PI in the VAD-TAH population (Brindle, 2019, unpublished data). Predictor variable selection for this study is further described in the systematic review. Following Institutional Review Board

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approval, an eight-year retrospective cohort study utilizing the Virginia Commonwealth University Health System Pauley Heart Center VAD-TAH database for study years 2010-2018 was performed. Study years 2010-2018 were selected due to known improvements made in the electronic health record (EHR) in 2010, enhancing PI reporting, and documentation. During this period, an informatics assessment of EHR accuracy for pressure ulcer documentation and staging reported an 89% positive predictive value (PPV) for pressure ulcer diagnosis and 94% PPV for pressure ulcer staging by clinical staff (unpublished data, VCU Health). Auto-consultation of PI expert certified wound-ostomy-continence nurses by the EHR to validate pressure ulcer diagnosis and staging further enhanced accuracy.

The study group included all ventricular assist device (Heartware-HVAD, Heartware International Inc., Framingham, MA; Heartmate II (HM 2) & Heartmate III (HM3), Thoratec-Abbott Laboratories, Abbott Park, IL) or total artificial heart surgeries (50-70cc TAH with companion or freedom driver, Syncardia, Tucson, AZ). Inclusion criteria included all patients undergoing VAD-TAH surgery, who were 18 years and older. Exclusion criteria included: 1) patients who did not receive cardiopulmonary bypass (off-pump procedures); 2) had VAD-TAH to orthotopic heart transplant surgery; 3) expired prior to postoperative day five; 4) pregnant women; 5) patients less than 18 years of age 6) department of corrections population and 7) patients who had pre-existing PI present on admission. Some subjects had multiple admissions for subsequent device surgeries during the study time-period, such as having a VAD replaced or transitioning from VAD to TAH. However, in all cases, these surgeries were months to years removed from the original surgery and therefore, all surgical events were admitted provided they met inclusion/exclusion criteria for each individual surgery. Due to the lack of available occurrence rates in the literature for PI in VAD-TAH patients, rule of thumb considerations were

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used for effect size and sample size requirements by allowing for at least 10 PI events per variable (20 total) indicating a necessary sample size of at least 200 patients for retrospective review (Kellar & Kelvin, 2012, p. 327; Lance & Vandenberg, 2009).

Measures

An existing research database created by the department of cardiac surgery at our university hospital was utilized for this research study. Research coordinators for the department were responsible for inputting data from the VCU Internal Quality Dataset into the VAD-TAH database. All (100%) of patients receiving VAD-TAH devices have been inputted into this database. The VAD-TAH database was provided via encrypted, password protected access to ensure confidentiality and accessed by the study PI after IRB approval on August 27th, 2018. The database was then deidentified using a heuristic method by the author (CTB) and patients were removed who were not in the study period of 2010-2018, or who were listed as having expired before post-operative day 5. The database was then augmented by adding the specific study variables to be investigated. All data was entered by the study principle investigator. Information bias was controlled using a data collection tool developed to guide the same process for data abstraction for each surgical case. Biological gender at birth (male or female) was recorded and ethnicity was defined as Caucasian, Black or African-American, Hispanic, or other. BMI was defined as underweight (<18.5), normal weight (18.6-24.9), overweight (25-29.9) and obese (>30). New York Heart Association Heart Failure Classification Scale was utilized to identify preoperative morbidity (1-4). Preoperative Braden Risk Assessment Scale scores were defined as low risk (23-18), medium risk (17-13) and high risk (<13) respectively. American Society of Anesthesiologist Score (ASA) were documented from anesthesiologist or certified registered nurse anesthetist pre-operative assessments. ASA scale scores range from I (mild systemic

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disease) to V (moribund patient not expected to survive without surgical intervention) (Dripps, Lamont, & Eckenhoff, 1961). Anxiety and depression were defined by preoperative diagnosis of the respective conditions within history and physical or diagnostic code. Total number of surgeries was recorded and defined as the total number of surgeries (all types) during a single admission. Operative time was defined in minutes from the recorded on-table through off-table times recorded in the OR record. Bypass times were defined in minutes and recorded from the on-pump through off-pump time recorded in the OR record. Mean arterial pressure time less than 60mmhg were recorded from OR anesthesia records and defined in minutes as displayed in 5-minute recorded segments. Aortic cross clamp time was taken directly from the surgeons' post-operative note in minutes. Time to chest closure was defined by the time in minutes from the end of the initial implant surgery until sternal closure (with or without skin closure) at the surgery end time of a subsequent procedure. Length of stay was recorded in days from admission to discharge from the hospital. Mechanical ventilation time was recorded in minutes from the initial intubation either before or during the surgical procedure until extubation. For patients who were reintubated shortly after 1st extubation, the time in minutes until subsequent successful extubation was added to the initial time. Total immobility time was defined as the time in minutes from last turn before surgery, to time of first turn after return to ICU (all VAD-TAH patients went straight from OR to ICU without stopping in post anesthesia care unit). PI were defined as preoperative (documentation of PI from time of admission to assessment during perioperative pre-surgical assessment), intraoperative (defined as a PI documented from first skin assessment post-operatively to post-operative day 5), and post-operative (defined as documentation of PI from post-operative day 6 through time of last skin assessment before discharge). PI were first classified by staff nurses and then validated by certified wound ostomy

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continence nurses using the updated 2016 National Pressure Ulcer Advisory Panel Pressure Ulcer Prevention and Treatment Guidelines (Edsberg, et al., 2016).

Data Analysis

PI incidence is reported by case-incidence and patient-incidence, defined as the number of new PI that developed divided by the total number of cases and total number of patients respectively. Incidence density is reported by associated years, defined by the number of new PI that develop during each1000 patient days over the study period. The primary null hypothesis for the study is that there are no differences between means comparing dichotomous PI groups (H1o: $\mu1=\mu2$) and the alternative hypothesis is that there are differences between group means (H1a: $\mu1\neq\mu2$). The secondary null hypothesis is that there are no differences between mean comparison of device types (H2o: $\mu HVAD=\mu HM2=\mu HM3=\mu TAH$) with an alternative stating there are differences (H2a: $\mu HVAD\neq\mu HM2\neq\mu HM3\neq\mu TAH$). Comparison of the presence of dichotomous preoperative diagnosis of anxiety or depression were compared to PI groups using Chi-square analysis respectively. An overall type I error of $\alpha = 0.05$ and type II error of $\beta=0.2$ was utilized. Missing data were left as missing and no imputation was performed. Descriptive statistics of the sample are reported by mean, standard deviation and 95% confidence intervals for normally distributed data and median and interquartile ranges for non-normally distributed data confirmed by QQ plots. Bivariate statistics comparing variables with the dichotomous dependent variable (pressure ulcer yes/no) were performed using Chi-Square for categorical variables and two-sample t-tests for continuous variables. Multivariate logistic regression of predictors against the dichotomous outcome variable was performed in three steps by data clumping of significant bivariate demographic and clinical variables separately, then entering all significant predictors

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into the final model. Per Hosmer and Leminshow's model, all predictors were included with p values of 0.25 or less and entered into the final model , where stepwise backward removal of predictors with $p > 0.05$ was performed until only significant predictors with $p < 0.05$ remained. Data are presented by mean, sample size, standard error, degrees of freedom, and odds ratio. Equality of error variance between the variables and dependent variable were checked for homoskedasticity. Cross product terms of related predictors were checked for multicollinearity. Separately, individual VAD-TAH device types were compared to continuous clinical variables using one-way analysis of variance (ANOVA) with post hoc Tukey HSD to investigate surgical procedure specific differences in group means.

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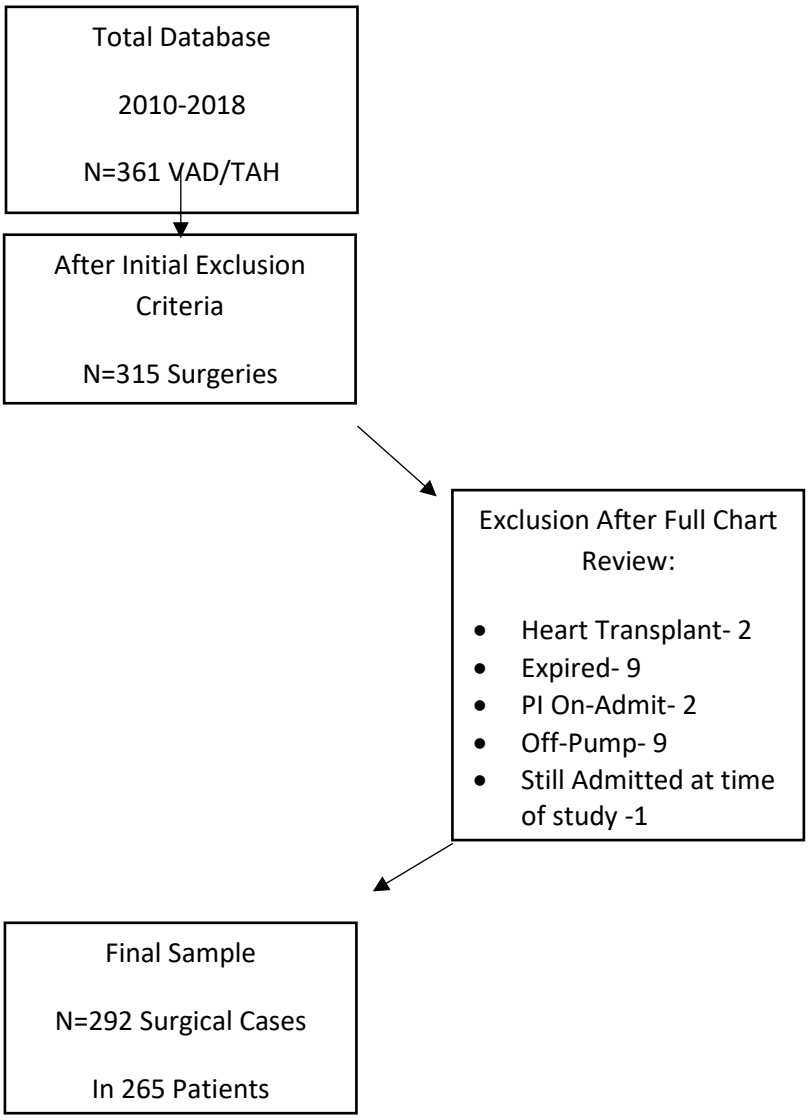
RESULTS

Figure 1. Case and Patient Inclusion Data



In total, 361 VAD-TAH cases were identified between study years 2010-2018. Following exclusions, the final sample for investigation included 292 independent VAD-TAH surgical cases conducted in 265 patients. In total, 32 patients developed 45 pressure ulcers. Despite some subjects having multiple surgical admissions during the study period, all pressure ulcers developed in individual patients during a single admission. The incidence of PI per all surgical cases was 11% (32/292), with PI incidence per patients of 12% (32/265). Incidence density was

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found to be (10/1000) 1% for 2010-2012, (12/1000) 1.2% for 2013-2015, and (10/920) 1.1% for 2016-2018 respectively. Mean hospital length of stay by device included 34.8 days for HVAD, 43.5 for HM2, 35.5 for HM3 and 108.6 days for TAH.

The distribution of all pressure ulcers by their period of development (preoperative, perioperative, post-operative >5 days) and mean time to ulceration are found in Table 1 and 2. Five pressure injuries developed in both the preoperative and intraoperative period respectively (1.7%), while 7.9% developed in the post-operative period. The mean time to ulceration for PI on all patients after admission was 28.3 days (n-32, μ=40,801.4 (mins) SD-36,140, 95% CI 27306.1-54,296.7) with secondary ulcers occurring on 13 of 32 patients, ulcerating at 23.9 days after admission (n-13, μ=34459.4 (mins), SD-33,828.6, 95%CI 14017.0-54,901.8). Following the end of the VAD-TAH implant surgery, median days to PI development was 13.7 days (n-27, median 19,712 (mins), IQR 8538-30649) and 11.2 days (n-9, median 16,135 (mins), IQR 8567.0-34244.5), reflecting the low rate of intraoperative development and high rate of post-operative ulceration respectively

TABLE 1. DISTRIBUTION OF ALL PRESSURE ULCERS BY DEVELOPMENT PERIOD PER CASE (VAD/TAH)

	Count	Proportion
No Pressure Ulcers	**258**	**88.7%**
Pre-Operative	**5**	**1.7%**
Intra-Operative	**5**	**1.7%**
Post-Operative	**23**	**7.9%**
Total	**291***	**100%**

*One patient had missing documentation of PI initiation and timing of presentation is unknown.

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TABLE 2. Mean Time to Ulceration: Admission and End of Operative Case

TIME UNTIL ULCERATION					
Variable	**n**	**Mean (Minutes)**	**SD**	**95% CI**	**Time Conversion: Days Until ulceration**
Admit to 1st Document (PI 1)	32	40801.4	36140.9	27306.1-54296.7	28.3
Admit to 1st Document (PI 2)	13	34459.4	33828.6	14017.0-54901.8	23.9
	N	**Median (Minutes)**	**IQR**		
OR End Until 1st Document (PI 1)	27	19712	8538-30649		13.7
OR End Until 1st Document (PI 2)	9	16135	8567.0-34244.5		11.2

Note: OR End to 1st Ulceration reflects only those 23 post-operative (1st occurring) pressure ulcers and secondary post-operative pressure ulcers occurring in patients with primary-preoperative and intraoperative pressure ulcers.

Comparison of Device Types

The distribution of PI by VAD and TAH are found in Table 3. Five VAD patients developed pressure ulcers in the preoperative and intraoperative period respectively with 16 in the post-operative period for a total of 26 patients out of 234 (11.1%). Six TAH patients developed post-operative pressure ulcers (6/56) or 10.7%. Univariate distributive statistics for surgical variables by device type are shown in Table 4, with one-way ANOVA comparison of

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means between surgical variables by device type in Table 5. Intraoperative variables included time parameters (indicative of potential ischemia/reperfusion potential) including total OR time, cardiopulmonary bypass time (CPB), mean arterial pressure time sustained at <60mmhg during the procedure, and aortic cross clamping time all in minutes. Total operating times were different between various devices. TAH OR times were significantly longer compared to HVAD (8.6 hours vs. 7.2 hours p=0.0002) and HM3 (8.6 hours vs. 7.3 hours p=0.0245) respectfully and HM2 times were significantly longer than HVAD (8.2 hours vs. 7.2 hours p=0.0024). No other differences between devices and OR times were noted. Cardiopulmonary bypass times (CPB) also differed significantly between TAH and all VAD types (TAH 207 min vs. HVAD 118.8 min, HM2 128.1 min, HM3 124 min, p=0.0001 respectively) however, there were no differences in CPB comparing the VAD devices (all p>0.7). Total time that mean arterial pressure (MAP) was below 60mmhg in minutes was compared by device type and showed significant variance between TAH and HVAD (21.6 vs. 7.2 minutes, p=0.0080), TAH and HM3 (21.6 vs. 1.7 minutes p=0.0089), HM2 and HM3 (16.7 vs. 1.7 minutes, p=0.0466). Intraoperative aortic cross clamping time varied between groups with significantly longer periods noted between TAH and HVAD (154.4 vs. 8.9 minutes, p<0.0001), TAH and HM3 (154.4 vs 17.2 minutes, p<0.0001) and HVAD and HM2 (8.9 vs 11.7 minutes, p=0.0001).

Post-operative surgical variables compared between device groups included total immobility time, mechanical ventilator time (minutes), time from surgery end to chest closure (minutes) and total length of stay in days by device. There were no significant differences noted in total immobility time or mechanical ventilator time between the respective devices. However, time to chest closure was significantly longer for TAH compared to HVAD (33.5 vs. 9.93 hours, p=0.0003) and HM3 (33.5 vs. 15.0 hours, p=0.0098) and TAH had significantly longer lengths

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of stay compared to all VAD types (all p<0.0001). There were no differences between VAD types respectively in either group for these variables.

Despite the disparity noted between the respective surgical variables above, the differences in PI occurrence between VAD-TAH groups was not significant (n=291, DF=2, χ^2=0.027, ρ=0.87) and there were no differences in PI development by operative period (pre/intra/post) between VAD-TAH patients (n-291, DF=3, χ^2=3.08, ρ=0.38). Therefore, PI risk by predictors was evaluated by dichotomous groups of PI vs. no PI patients, irrespective of device.

TABLE 3. DISTRIBUTION OF PRESSURE ULCERS BY IMPLANT TYPE

		Operative Development Period		
Device Type	**Total Pressure Ulcers**	**Pre**	**Intra**	**Post**
VAD	**26/234 (11.1%)**	**5**	**5**	**16**
TAH	**6/56 (10.7%)**	**0**	**0**	**6**

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TABLE 4. Distributive Statistics of Time Variables by Device Type

VARIABLE	HVAD				Heartmate II				Heartmate III				TAH			
Time-Minutes (hrs.)	**N**	**Mean (Minutes)**	**SD**	**95% CI**	**N**	**Mean (Minutes)**	**SD**	**95% CI**	**N**	**Mean (Minutes)**	**SD**	**95% CI**	**N**	**Mean (Minutes)**	**SD**	**95% CI**
OR Time (hrs.)	64	434.6 (7.2)	111.9	406.7-462.6	148	491.2 (8.2)	98.1	475.3-507.2	21	437.71 (7.3)	140.7	373.7-501.8	58	514.6 (8.6)	105.2	486.9-542.2
CPB Time	63	118.8	60.7	103.49-134.07	148	128.1	54.8	119.18-137.0	22	124.0	76.4	90.08-157.83	57	207	78.4	186.19-227.81
MAP Time in OR<60mmhg	63	7.2	13.9	3.7-10.7	147	16.7	26.0	12.5-20.9	21	1.7	5.8	-0.9-4.3	58	21.6	33.0	13.0-30.3
Cross Clamp Time	64	8.9	29.2	1.6-16.8	148	11.7	31.2	6.7-16.8	22	17.2	39.0	-0.1 - 34.5	57	154.4	76.5	134.1-174.7
Total Immobility Time	64	1313.8 (21.9)	1277.3	994.8-1632.9	148	1273.1 (21.2)	913.4	1124.7-1421.5	22	1063.5 (17.7)	832.2	694.6-1432.5	56	1419.7 (23.7)	664.0	1241.8-1597.5
Time OR End to Chest Closure	64	595.8 (9.93)	1339.7	261.1-930.4	148	1265.1 (21.1)	2212.5	905.7-1624.5	22	901.8 (15.0)	192.3	100.4-900.1	58	2012.5 (33.5)	1920.2	1507.6-2517.4
Length of Stay (LOS) Days	64	34.8	19.3	30.0-39.6	148	43.5	26.1	39.3-47.8	22	35.5	24.6	24.6-46.4	58	108.6	85.0	86.2-130.9
	N	Mean (Minutes)	SD	95% CI	N	Mean (Minute)	SD	95% CI	N	Median (Minute)	IQR		N	Mean (Minutes)	SD	95%CI
Mechanical Vent Time	64	6016.5	10573.4	3375.3-8657.7	148	6733.7	8366.7	5374.6-8092.9	21	1711	726-5155.5		58	11893.1	27329.8	4707.1-19079.1

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(hrs.)		(100.3)				(112.2)				(28.51)				(198)		

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TABLE 5 (A-G). ANOVA Comparison of Means for Surgical Variables by Device Type

A--OR Time by Device Type

Device	Device	Difference	SE	Lower CL	Upper CL	p-Value
TAH	HVAD	79.9	19.2	30.22	129.63	0.0002*
TAH	HM 3	76.8	27.0	7.02	146.65	0.0245*
HM2	HVAD	56.6	15.9	15.60	97.62	0.0024*
HM 2	HM 3	53.5	24.7	-10.40	117.45	0.1360
TAH	HM 2	23.3	16.4	-19.15	65.78	0.4887
HM 3	HVAD	3.08	26.7	-65.85	72.03	0.9994

B--CPB Time by Device

Device	Device	Difference	SE	Lower CL	Upper CL	p-Value
TAH	HVAD	88.2	11.5	58.4	118.0	<.0001*
TAH	HM 3	83.0	15.8	42.1	124.0	<.0001*
TAH	HM 2	78.9	9.8	53.5	104.3	<.0001*
HM 2	HVAD	9.3	9.5	-15.2	33.8	0.7603
HM 3	HVAD	5.2	15.6	-35.2	45.5	0.9874
HM 2	HM 3	4.1	14.4	-33.1	41.4	0.9918

C--Mean Arterial Pressure Time in OR <60mmhg By Device Type

Device	Device	Difference	SE	Lower CL	Upper CL	p-Value
TAH	HM 3	20.0	6.3	3.7	36.2	0.0089*
HM 2	HM 3	15.0	5.8	0.2	29.9	0.0466*
TAH	HVAD	14.4	4.5	2.8	26.0	0.0080*

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HM 2	HVAD	9.5	3.7	-0.1	19.1	0.0546
HVAD	HM 3	5.6	6.2	-10.5	21.6	0.8083
TAH	HM 2	4.9	3.8	-5.0	14.8	0.5700

D--Cross Clamp Time by Device Type

Device	Device	Difference	SE	Lower CL	Upper CL	p-Value
TAH	HVAD	145.5	8.0	124.8	166.2	<.0001*
HVAD	HM 2	142.7	6.9	124.9	160.4	<.0001*
TAH	HM 3	137.2	11.1	108.7	165.8	<.0001*
HM 3	HVAD	8.3	10.9	-19.9	36.4	0.8722
HM 3	HM 2	5.4	10.1	-20.6	31.4	0.9489
HM 2	HVAD	2.8	6.6	-14.2	19.9	0.9734

E--Total Immobility Time by Device Type

Device	Device	Difference	SE	Lower CL	Upper CL	p-Value
TAH	HM 3	356.1	241.8	-268.8	981.1	0.4555
HVAD	HM 3	250.3	237.5	-363.6	864.1	0.7180
HM 2	HM 3	209.6	219.6	-358.0	777.1	0.7755
TAH	HM 2	146.6	150.8	-243.1	536.3	0.7655
TAH	HVAD	105.9	175.9	-348.6	560.4	0.9314
HVAD	HM 2	40.7	143.8	-330.9	412.3	0.9921

F--Mechanical Ventilator Time by Device Type

Device	Device	Difference	SE	Lower CL	Upper CL	p-Value
TAH	HM 3	7864.2	3697.1	-1689.8	17418.2	0.1470
TAH	HVAD	5876.6	2631.8	-924.4	12677.6	0.1169
TAH	HM 2	5159.3	2248.9	-652.1	10970.8	0.1018

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HM 2	HM 3	2704.9	3385.1	-6042.9	11452.7	0.8548
HVAD	HM 3	1987.6	3650.8	-7446.6	11421.9	0.9480
HM 2	HVAD	717.2	2171.8	-4895.1	6329.6	0.9876

G--Time OR End to Chest Closure by Device

Device	Device	Difference	SE	Lower CL	Upper CL	p-Value
TAH	HM 3	1512.3	480.3	271.0	2753.6	0.0098*
TAH	HVAD	1416.8	347.8	518.0	2315.5	0.0003*
HM 2	HM 3	764.8	438.3	-367.9	1897.6	0.3025
TAH	HM 2	747.5	297.2	-20.5	1515.4	0.0597
HM 2	HVAD	669.3	287.0	-72.4	1410.9	0.0932
HVAD	HM 3	95.6	474.1	-1129.6	1320.7	0.9971

PRESSURE ULCER RISK FACTORS, STAGE & LOCATION

The stage and location of all 45 pressure ulcers that developed during the study period are reported in Table 6. The most common stage of pressure ulcer identified was deep tissue injury (DTI), representing 44% of all ulcers. The remainder included mucosal injuries (22%), stage 2 (17.7%), unstageable (8.9%), and stage 3 (6.7%). There were no stage 1 or stage 4 pressure ulcers documented. The most common locations for occurrence included the buttocks (24.4%), the coccyx (15.6%), and the lip (11.1%). The sacrum, occiput and nares all developed 3 pressure ulcers in the 8-year study period (6.7%), whereas the heel, ischium and breast (all 2.2%) were the least reported. Of note, 13 of 45 ulcers were directly attributed to corresponding medical devices (28.8%) including nasogastric tubes, endotracheal tubes, and post-surgical bra.

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TABLE 6. Distribution of Pressure Ulcers by Stage and Location

45 Pressure Ulcers Presented in 23 Total Patients												
			Group 2: Pressure Ulcer									
Stage	**Freq**	**%**	**Locations**									
			Buttocks	**Coccyx**	**Heel**	**Ischium**	**Sacrum**	**Breast**	**Occiput**	**Nare**	**Lip**	**Ear**
1	0	0	0	0	0	0	0	0	0	0	0	0
2	8	17.7%	3	2	0	0	0	1	0	0	0	1
3	3	6.7%	0	1	0	1	1	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
DTI	20	44.4%	7	4	1	0	2	0	1	0	0	0
Unstageable	4	8.9%	1	0	0	0	0	0	2	1	0	0
Mucosal	10	22.2%	0	0	0	0	0	0	0	2	5	1
Total	45	100%	11	7	1	1	3	1	3	3	5	2
	% Location		24.4%	15.6%	2.2%	2.2%	6.7%	2.2%	6.7%	6.7%	11.1%	4.4%
Device Related?	13	28.8%										

Univariate statistics of the predictor variables and bivariate chi-square comparison of dependent variable groups are shown for categorical variables in Table 7 and continuous variables by t-test in Table 8. Comparison of demographic variables demonstrated no differences between gender, ethnicity, or smoking history in the 6 months prior to surgery for patients with and without PI. Additionally, baseline clinical diagnoses of diabetes, anxiety, depression, New York Heart Association (NYHA) heart failure classification, American Society of Anesthesia (ASA) score and use of intravenous corticosteroids preoperatively did not differ between patients with and without PI. However, significant differences were identified in three categorical variables including basal metabolic index (n-291, DF-3, χ^2=11.6, p=0.0088), preoperative Braden Risk assessment scores (n-290, DF-3, χ^2= 25.78, p<0.0001), and the occurrence of

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myocardial infarction during admission (n-290, DF-1, χ^2=18.64, p<0.0001). In total, five continuous variables were found to be significantly different between PI groups, including: age (t- 3.52, DF 42.5, 95% CI 3.4-12.6, p-0.001), length of stay in days (t-2.45, DF 35.7, 95% CI 5.4-57.1, p-0.019), total immobility time in minutes (t-2.8, DF 35.6, 95% CI 186.4, 1163.1, p=0.0081), mechanical ventilation time in minutes (t- 2.12, DF 32.5, 95% CI 855.5- 25413.3, p=0.037) and the total number of surgeries (t-2.33, DF 37.8, 95%CI 0.11- 1.61, p=0.025). Interestingly, there were no differences noted between patients with and without PI with respect to: total OR time, CPB time, time MAP <60mmhg, open chest time, aortic cross clamping time or the total days from admission prior to implantation of the device.

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TABLE 7. Bivariate Comparison of Categorical Variables to Dependent Variable Groups

Group 1: NO-PI				Group 2: YES- PI		Comparison Chi-Square
CATEGORICAL VARIABLES						
Variable	**Freq**	**%**		**Freq**	**%**	
Gender						n-291, DF 2, χ^2= 0.390
Male	193	74.8		25	78.1	p= 0.82
Female	65	25.2		7	21.9	
Ethnicity						n-289, DF 4, χ^2=2.15, p=0.71
Caucasian	120	46.6		18	56.2	
Black-A.A.	128	49.4		14	43.8	
Hispanic	6	2.3		0	0	
Other	4	1.6		0	0	
BMI						n-291, DF 3, χ^2=11.6, p=0.0088
Under wt.<18.5	5	1.9		2	6.3	
Normal wt. (18.6-24.9)	39	15.1		11	34.4	

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Over wt: (25-29.9)	59	22.9		9	28.1	
Obese: >30	155	60.1		10	31.3	
DM						n-290, DF 1, χ^2=0.25, p=0.62
No	149	57.8		17	53.1	
Yes	109	42.2		15	46.9	
Anxiety						n-290, DF-1, χ^2=0.194, p=0.66
No	236	91.5		30	93.8	
Yes	22	8.5		2	6.2	
Depression						n-290, DF-1, χ^2=0.845, p=0.36
No	238	92.2		28	87.5	
Yes	20	7.8		4	12.5	
NYHA						n-289, DF 3, χ^2=5.27, p=0.15
Class 1	3	11.7		2	6.3	
Class 2	3	11.7		1	3.1	
Class 3	115	44.9		12	37.5	
Class 4	135	52.7		17	53.1	
Pre-Op Braden						n-290, DF-3, χ^2= 25.78, p<0.0001

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Low Risk (23-18)	191	73.9		12	37.5	
Med. Risk (17-13)	55	21.3		12	37.5	
High Risk (<13)	12	4.7		8	25.0	
IV Corticosteroids						n-290, DF-1, χ^2=0.50, p=0.48
No	254	98.5		32	100	
Yes	4	1.5		0	0	
Smoker <6 Months						n-290, DF-1, χ^2=3.259, p=0.07
No	230	89.1		25	78.1	
Yes	28	10.9		7	21.9	
Type of Implant						n-290, DF-3, χ^2=1.82, p=0.61
HVAD	58	22.5		5	15.6	
Heartmate 2	131	50.8		16	50.0	
Heartmate 3	18	6.9		4	12.5	
Total Artificial Heart	51	19.8		7	21.9	

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Cardiac Arrest During Stay				Blank page?	n-290, DF-1, χ^2=18.64, p<0.0001
No	232	90.3	21	63.6	
Yes	25	9.7	12	36.4	
ASA Score					n-290, DF-2, χ^2=5.09, p=0.08
1	0	0	0	0	
2	0	0	0	0	
3	19	7.4	2	6.1	
4	229	89.1	27	81.8	
5	9	3.5	4	12.1	

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TABLE 8. Bivariate Comparison of Continuous Variables by Dependent Variable Groups

CONTINOUS VARIABLES									
	Group 1: No Pressure Ulcer				Group 2: Pressure Ulcer				Group Comparison
Variable	**n**	**Mean**	**SD**	**95% CI**	**n**	**Mean**	**SD**	**95% CI**	**T-Test**
Age	258	51.91	13.35	50.3-53.6	33	59.94	12.16	55.6-64.3	**t- 3.52, DF 42.5, 95% CI 3.4-12.6, p-0.001**
Days-Admit to Implant	258	9.17	8.88	8.09-10.26	33	10.09	6.25	7.87-12.30	t-0.75, DF 50.2, 95% CI -1.53 – 3.37, p=0.46
LOS-Days	258	50.44	47.35	44.63-56.24	33	81.73	71.25	56.46-106.99	t-2.45, DF 35.7, 95% CI 5.4-57.1, p-0.019
OR Anesth Time (min)	257	475.27	108.95	461.89-488.66	33	514.09	112.24	474.29-553.88	t-1.88, DF 40.1, 95% -3.0 -80.6, p=0.07
CPB Time (min)	256	138.97	69.83	130.38-147.57	33	160.97	76.31	133.91-188.03	t- 1.57, DF 39.2, 95% CI -6.3, 50.3, p=0.12
Total Immobility (mins)	256	1217.44	874.54	1109.8-1325.1	33	1892.18	1346.48	1414.74-2369.62	t-2.8, DF 35.6, 95% CI 186.4, 1163.1, p=0.0081

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Cross Clamp (Mins)	257	38.87	71.79	30.05-47.69	33	45.33	73.33	19.33-71.33	t-0.48, DF 40.3, 95% CI -20.9, 33.8, p=0.64
OR-MAP <60 mmhg (mins)	256	13.67	24.05	10.71-16.63	32	21.88	33.35	9.85-33.90	t-1.35, DF 35.1, 95% CI -4.1, 20.56, p=0.19
OR-Chest Close (Mins)	258	1141.8	1929.5	905.29-1378.40	33	1772.6	2257.1	972.24-2572.92	t- 1.54, DF 38.2, 95% CI -200.9, 1462.3, p=0.13
Mech Vent Time (mins)	257	5935.38	8588.03	4880.42-6990.33	33	19069.79	34513.32	6831.9-31307.68	t- 2.12, DF 32.5, 95% CI 855.5-25413.3, p=0.037
Total # Surgeries	258	2.14	1.67	1.93-2.34	33	3	2.03	2.28-3.72	t-2.33, DF 37.8, 95%CI 0.11- 1.61, p=0.025

To determine the predictor variables for pressure injury development in the VAD-TAH population, the respective significant bivariate comparisons were entered into a multivariate, backward, stepwise regression model with results reported in Table 9. The final model suggests that age (df-1, χ^2=9.91, p=0.0016), pre-operative Braden Score (df-3, χ^2=15.88, p=0.0012) and mechanical ventilation time (df-1, χ^2=8.43, p=0.0037) are all significant predictors of PI in the VAD-TAH population. Odds ratio indicate for a unit change in age, the odds for pressure ulcer development are expected to increase by a factor of 1.06 (95% CI 1.02-1.09). For mechanical

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ventilation time, for each unit change in minutes, the odds for pressure ulcer development are expected to increase by a factor of 1.00 (95% CI 1.000003-1.000067) holding all other variables constant. Preoperative Braden scores were dummy coded on three levels of risk: 0-Low Risk (23-18), 1-Medium Risk (17-13) and 2-High Risk (<13). Between risk groups, the odds of developing a PI are 3.73 times higher when a patient is medium risk compared to low risk (F_1, df-3, χ^2=15.88, 95% CI 1.52-9.13, p=0.0040) and 9.21 times higher risk of developing a PI when a patient is considered high risk compared to low risk (F_1, df-3, χ^2=15.88, 95% CI, 2.79-30.39, p=0.0003).

Table 9. Multivariate Logistic Regression of Significant Predictors and Odds Ratios

Variable	Nparm	DF	ChiSquare	p-value	Odds Ratio	Lower 95%	Upper 95%
Age	1	1	9.91	0.0016	1.06	1.02	1.09
Mech Vent T	1	1	8.43	0.0037	1.00	1.00	1.00
Braden 0(23-18) 1-(17-13) 2-(<13)	3	3	15.88	0.0012			
Braden 1:0				0.0040	3.73	1.52	9.13
Braden 2:0				0.0003	9.21	2.79	30.39
Braden 0:1				0.0040	0.27	0.11	0.66
Braden 0:2				0.0003	0.11	0.033	0.36

DISCUSSION

This study represents the first investigation of the development of PI in patients undergoing ventricular assist device or total artificial heart surgeries. In this retrospective

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analysis, age, mechanical ventilation time and preoperative Braden Risk Assessment Score were the only significant predictors of PI development across all devices. Age is associated with a higher risk for PI development in multiple studies of cardiac surgery patients and is associated with risk during operative procedures, possibly related to physiologic and anatomical changes associated with increasing age such as muscle atrophy, rete-peg-papillary-dermis flattening and increasing tissue hypoxia (Chen, Shen, Xu, Zhang, & Wu, 2015; Cox, 2011, 2011; Feuchtinger et al., 2005; Halfens, Van Achterberg, & Bal, 2000; Lindgren, Unosson, Fredrikson, & Ek, 2004; Lumbley, Ali, & Tchokouani, 2014; Manzano et al., 2010; O'Brien et al., 2014; Papantonio, Wallop, & Kolodner, 1994; Perneger et al., 2002; Sewchuk, Padula, & Osborne, 2006; Slowikowski & Funk, 2010; Webster et al., 2011). Age related changes may impair tissue tolerance secondary to decreased tissue integrity during tissue loading and exacerbate the inflammatory response to injury. In bivariate analysis, this study shows that patients who developed PI were older than those patients without PI development (t-3.52, DF 42.5, 95% CI 3.4-12.6, p-0.001). Additionally, the study suggests that patients who developed PI spent significantly longer time on mechanical ventilation than those without PI (mean 13.24 days vs. 4.12 days; 2.12, DF 32.5, 95% CI 855.5- 25413.3, p=0.037). Mechanical ventilation represents a risk for PI development secondary to prolonged head of bed elevation greater than 30 degrees, decreased mobility, and represents potential host complications in systemic tissue oxygenation. When considering age and mechanical ventilation in multivariate analysis, however, the low odds ratios (age OR= 1.06; mech vent OR=1.00) suggest a 50-50 chance of developing PI for each predictor. However, when considering Braden Risk Assessment Score, the most significant predictor of PI was a Braden score indicative of high risk or <13, indicating 9 times greater odds for PI between high risk versus low risk patients preoperatively (p-0.0003, OR 9.21, 95% CI 2.79-30.31). While patients with normal Braden Scores preoperatively are still in jeopardy of PI due to factors associated with the aforementioned operative and post-operative risks, patients with existing challenges in mobility, friction/shear, moisture, activity level, nutrition and sensory perception will be exacerbated by prolonged operating room and post-operative recovery periods demonstrated in the

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various device types. Interestingly, however, the overall incidence density (1-1.2%) and patient incidence of 12.1% for this study is remarkably low given the historical rates of pressure ulcers reported in other non-device cardiac surgery studies.

The VAD-TAH procedure is more invasive and has greater operating room times than CABG (3-6 hours) (Cotts, McGee, Myers, Naftel, Young, Kirklin & Grady , 2014) compared to 7.2-8.6 hours shown in this study. Additionally, average LOS for CABG surgery is five days (Cotts et al., 2014; (El Banayosy, Kizner, Arusoglu, Morshuis, Brehm, 2014), while VAD and TAH average LOS ranged between 19.3 and 108.6 days in this study. Next, VAD-TAH patients are further at risk due to more advanced heart failure with severely reduced cardiac function, whereas CABG patients have coronary artery occlusion with or without existing heart failure. This differentiation is significant because patients with advanced left ventricular failure or biventricular failure requiring VAD-TAH have significantly higher preoperative Anesthesia Severity Assessment (ASA) scale scores compared to CABG patients based upon their advanced HF. ASA scores greater than or equal to three are associated with higher operating room pressure ulcer rates (O'Brien, Shanks, Talsma, Brenner, & Ramachandran, 2014). For each one point increase in ASA, the odds of developing PI have been reported to increase by 149% (Fred, Ford, Wagner, & Vanbrackle, 2012). This is significant because the VAD-TAH patients in this study were: ASA-3 (7.4%), ASA-4 (89.1%), ASA-5 (3.5%) indicating severe heart failure and high surgical risk.

Additionally, this study presents the first attempt to capture total immobility time to account for cumulative preoperative, intraoperative and post-operative immobility to gauge the total supine ischemic, compression and deformation strain potential, exerted on the soft tissue of these patients. As time under compression and tissue strain reflect the potential extent of direct

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tissue damage and potential severity of reperfusion injury, identification of surgical risk should not be confined to the time on the operating table alone. While CABG patients tend to have same-day progressive mobility practices which limit immobility after surgery, the VAD-TAH patients in this study averaged a staggering 21.2-23.7 hour of complete supine immobility and averaged 2.14-3 operations per patient, per admission. Yet again, the overall incidence of PI, especially in dependent bony prominences of the supine patient were less than expected. Reasons for extended immobility in this study were attributed to active bleeding, hemodynamic instability, and cardiac arrest. The difference between PI groups was significant for total immobility time in bivariate modeling (t-2.8, DF 35.6, 95% CI 186.4, 1163.1, p=0.0081) though not significant in the final multivariate model. Of interest, as hemodynamic instability is often a subjective determinant of patient positioning, it should be noted that the cardiac surgery ICU protocols for aggressive turning and positioning utilized during the study duration have been previously published (Brindle, Malhotra, O'Rourke, Currie, Chadwick, Falls, et al., 2013). While adherence to these protocols was not measured in this study, a previous description of the effectiveness of these prevention practices specific to this cardiothoracic ICU was published (Cooper, Jones, & Currie, 2015). The authors described trends toward decreased PI rates despite increasing patient acuity and increasing numbers of extracorporeal membrane oxygenation use (ECMO) displaying a heightened culture of prevention and implementation of successful protocols in practice.

In this study, not only was there a low rate of PI incidence, but most of the ulcerations developed after the intensive care unit (ICU) stay. Theoretically, most patients in this study remained pressure injury free through surgery, prolonged immobility, and vasopressors to control labile hemodynamic periods in the ICU, until a point at which they ulcerated, where

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traditionally the patient would have been considered to be at lower risk compared to the perioperative through intensive care period. The large majority of PI development in the buttocks may reflect the high BMI habitus (60.1% BMI >30 vs. 31.3% BMI >30 in PI vs. no-PI groups; n-291, DF 3, χ^2=11.6, p=0.0088) of the patients in this study which naturally increases the loading and deformation of the buttocks tissues in comparison to the sacrum or ischium. In addition, Sprigle and Sonenblum recently described the relative differences in tissue thickness, deformation and frictional forces dependent upon the level of head of bed elevation compared to PI morphology (Sprigle & Sonenblum, 2019). In this study, mechanical ventilation time was a significant predictor of PI and during this period, the standard of practice is to maintain head of bed elevation at 30 degrees. However, it was not possible to measure exact head of bed angle or periods of different positions in the supine state which should be considered in future studies as it may impact tissue tolerance.

Tissue tolerance, a concept specific to PI development, is multifactorial and refers to the susceptibility of developing a PI (Bhargava et al., 2014; Braden & Bergstrom, 1987; Coleman et al., 2014; Defloor, 1999). Tolerance of the individual tissues is defined by: 1) mechanical properties of tissue, 2) geometry (morphology) of the tissues and bones, 3) physiology and repair, and 4) transport of thermal properties (Coleman et al., 2013, 2014; Haesler, 2014). Therefore, a patient has a *baseline capacity to respond to the negative impact of the forces leading to tissue injury*, otherwise referred to as *tissue tolerance*. During hospitalization for cardiac surgery, the patient suffers repetitive tissue injuries from pressure and shear, each one exacerbating inflammation and structural damage within the tissue. This results in both an imbalance between available oxygen, metabolic demand for oxygen, and the build-up of oxygen free radicals (oxidative stress). Ultimately, if the frequency, duration, intensity, and repetitive

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nature of pressure and shear injuries overwhelms the hosts ability to respond using reparative mechanisms, a PI may develop. The capacity of the patient to respond to inflammatory tissue damage and oxidative injury following pressure and shear events determines the progression of tissue injury and potential for and severity of cutaneous manifestation. Rao and colleagues referred to this specifically as a tissue tolerance for oxygen (2016). The patient then enters repeating cycles of pressure and shear events as they suffer further from periods of immobility in the ICU, elevated head of bed positions, immobility during diagnostic tests, and multiple surgical procedures, among others, depending on the patient's condition. These subsequent events increase the damage caused by pressure and shear induced IR injury as the patient's post-injury tissue tolerance is less capable of mitigating repeated oxidative insults to the damaged tissue. A patient undergoing cardiac surgery typically has multiple comorbidities such as advanced heart disease, impaired cardiac output or systemic perfusion/oxygenation, decreased mobility, polypharmacy, et al., which impacts the body's ability to respond to insults and reduces overall tissue tolerance.

Potential Preventive Mechanisms

Two potential explanations for PI mitigation in this study include possible intrinsic and extrinsic factors. First, it is unknown what the impact of post-operative tissue perfusion changes are in the VAD-TAH patient. With immediate and considerable improvement in post-operative cardiac output following device implantation compared to that of the preoperative diseased heart, it is possible that tissue perfusion improved over their baseline HF state which provided improved circulation to at risk tissues. However, measuring blood pressure may be problematic especially in VAD patients due to reduced or absent pulse pressure with non-pulsatile flow. With these devices, pump speed is controlled by the clinician and increases in speed correspond to

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increased left ventricular unloading, cardiac output and end-organ perfusion (Aissaoui et al., 2018). In future prospective studies, it would be valuable to measure perfusion of the dependent tissues at risk for PI using ultrasound, hyperspectral and thermographic imaging or potentially with more invasive techniques.

Next, the patients in this study benefitted from a robust, PI prevention program that spanned the continuum of care from admission, through the surgical procedure and during their extended stay. All patients admitted to the ICU both before and after surgery were placed on alternating low air loss (LAL) mattress on admission as standard of care. In addition, staff followed an extensive ICU prevention protocol that included heel offloading devices, prophylactic 5-layer foam dressings, turning and positioning systems, moisture wicking incontinence pads, skin moisturizers and barriers and fluidized positioners. In addition, nursing and respiratory therapy staff participated in joint medical device related PI prevention protocols with built in EHR guidance for preventive interventions based on Braden Scale sub-score risk. The high rate of device related pressure injuries found in this study may reflect the total number of devices these patients come out of surgery with, unknown adherence and consistency in implementing the prevention protocol and the challenge to prevent these injuries. While there was a device prevention protocol in place, a number of factors may lead to device PI development despite a prevention protocol such as: 1) high number of devices per patient, 2) competing demands and ability to access/view skin under devices, 3) device manufacturing and construction using rigid materials, 4)lack of sufficient evidence to guide prevention with all types of devices 5)role confusion between interprofessional staff as to who is managing devices, 6) inability to remove or offload devices due to life threatening or anatomically specific, individual patient needs. In the operating room, all supine patients in cardiac surgery OR were on 4-inch

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viscoelastic foam mattresses that accommodated bariatric and normal BMI patients alike. In addition, patients had 5-layer prophylactic sacral foam dressings, fluidized positioners for protection of the occiput and either utilized heel offloading devices or 5-layer foam prophylactic heel dressings. After surgery, the patients were immediately transferred back onto their alternating pressure LAL mattresses. When transferred to step-down or on the general device floor, all beds continued to be either group-two static air mattresses or combination multilayer foam and air mattresses as the standard of care. The step-down and general floors similarly had prevention protocols which guided individualized prevention once the patient was out of the ICU. Due to the culture of prevention established across the organization, it is possible that the low rates of PI could be attributed to a high organizational awareness of risk and consistency in implementing preventive interventions. Therefore, the results shown in this study may not be generalized across other VAD-TAH operating organizations and should be compared to prospective studies in different facilities.

Biobehavioral Factors

One study aim was to determine whether there was a difference between preoperative diagnosis of anxiety and depression on PI development between groups. In this study, preoperative diagnosis of depression and anxiety were not found to be significant risk factors in either group (depression n-290, DF-1, χ^2=0.845, p=0.36; anxiety n-290, DF-1, χ^2=0.194, p=0.66). Depression and anxiety were investigated as cofactors in this study because they are prevalent conditions in the VAD-TAH population (17% and 42% respectively) (Huffman, Celano, & Januzzi, 2010) compared to non-device cardiac counterparts (Estep, Starling, Horstmanshof, Milano, Selzman, et al., 2015; Reynard, Butler, McKee, Starling, & Gorodeski, 2014; Shapiro, Levin, & Oz, 1996; Snipelisky, Stulak, Schettle, Sharma, Kushwaha & Dunlay,

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2015). Additionally, depression and anxiety are suggested to be associated with increased PI risk (Braden, 1998; Krause & Broderick, 2004; Krueger, Noonan, Williams, Trenaman, & Rivers, 2013). Thus, levels of depression and anxiety and the associated level of allostatic load, may biologically contribute to PI risk in cardiac surgery patients through the following mechanisms:

1. exacerbating the response to cellular damage and inflammation resulting from ischemia
2. exacerbating control of subsequent re-injury during reperfusion which causes oxidative stress, DNA damage and apoptosis in the skeletal muscle
3. alteration of systemic and cellular temperature exacerbating both ischemia and inflammation (Bhargava, Chanmugam, & Herman, 2014)
4. care factors such as adherence to rehabilitation plans (turning, walking, repositioning) thereby increasing immobility time (Shapiro et al., 1996).

However, the limitations of this study were the unknown practice of anesthesia and surgical providers on routine preoperative screening for depression and anxiety. As only a diagnostic code could be found in the patient's problem list, the accuracy of identifying depression and anxiety in a retrospective design is questionable. In future studies, prospective collection of the generalized anxiety disorder 7-item (GAD-7) scale and the patient health questionnaire-9 (PHQ-9) should be considered, as they are sensitive tools for the preoperative setting, are valid and reliable in the cardiac population and may predict cardiac mortality (Abed, Kloub, & Moser, 2014; Reynard et al., 2014). By utilizing these preoperative screening tools, the presence and *severity* of anxiety and depression could be modeled to gauge PI association. In addition, consideration for active pharmaceutical interventions before and after surgery may similarly be used as an indicator of the severity of these conditions in the future.

LIMITATIONS

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The limitations of this study include the retrospective design and availability of data within the medical record. Additionally, as there were no previous studies to guide selection of cofactors for PI in the VAD-TAH population, a surrogate population of non-device cardiac surgery patients guided variable selection (Brindle, 2019 in press). The inherent selection bias associated with surrogate population study selection, likely led to a lack of inclusion for other important cofactors. For example, Cox and Roche (2015) identified an incidence of 13% (41/306) in a retrospective correlational study of 306 patients in a medical surgical and cardiac surgical ICU. Of these pressure ulcers, 39% were DTPI and 56% were found on the sacrum. The authors identified significant risk factors specifically related to vasoactive medications with pressure ulcer patients having significantly longer infusion times of vasopressin (32 hours vs 87 hours, p=0.005) and longer infusion times of high dose vasopressin (20 hours vs. 57 hours, p=0.03) as significant in PI development (X^2=39.3, p<0.001). The authors specifically commented that the dose of 0.03 U/min may be a tipping point for pressure injury development. In this study, vasopressor utilization and dose were not captured and may have a significant role in risk for PI in VAD-TAH patients given the multiple medications and considerable dose experienced by these patients. Future prospective studies should capture drug type, dose, and duration during the preoperative through post-operative period.

Additionally, diabetes mellitus has been described as a significant predictor of operative PI in multiple studies but did not find significance in this study. Liu and associates (2012) performed a meta-analysis of six studies (4 cardiac surgery, 2 mixed surgical populations) of 2453 patients who had surgery, to investigate the effect of diabetes mellitus (DM) on the development of PI during surgical procedures. The incidence rate across studies was 11.8%, with no significant heterogeneity (X^2_5 =1.98, p=0.85, I^2=0%) between the studies. All studies were

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listed as IIB evidence and scoring a 7/8 for quality according to the Newcastle-Ottawa scale. The meta-analysis revealed that diabetes mellitus was significantly associated with the development of PI (OR 2.15 (95%CI: 1.62-2.84; Z-5.32, p<0.00001, fixed effects model OR=2.13). Even after the removal of one retrospective study, the odds were still found to be significant (OR=2.03) (Liu, He, & Chen, 2012). These findings were supported by a second meta-analysis of 13 studies including total comparison groups of patients with pressure ulcer (n=2367) and patients without (n=12053) showing DM to be a significant risk factor across surgical types with a pooled odds ratio of 1.74 (95%CI= 1.40-2.15, I^2=51.1%) (Kang & Zhai, 2015). When isolating the four studies involving cardiac surgery patients alone, DM remained a significant risk factor (OR=2.0, 95%CI=1.42-2.82, I^2= 0%). In this study, only a dichotomous inclusion of diabetes yes/no was included in the database as level of diabetes control evaluated by HgA1c was not recorded on all patients. In future prospective studies, evaluation of HgA1c may provide more depth of association by allowing for comparison of the dependent variable with the severity of the disease state. Finally, due to retrospective design there was no ability to utilize recently published operative risk assessment tools for intraoperative PI such as the Munro Scale or the American Operating Room Nurses Association Preoperative Risk Assessment Toolkit (Munro CA, 2010; "Prevention of Perioperative Pressure Injury Tool Kit - AORN," n.d.)

The low incidence of PI events in this study limit the ability to identify potentially significant variables. The research was conducted at a single, academic university quaternary medical center which limits generalizability. Finally, as PI prevention protocol adherence was not measured in this study, it is difficult to gauge whether the outcomes were associated with patient care factors or underlying physiologic protection.

CONCLUSION

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The overall incidence of pressure injury in this study was much lower than anticipated given historical incidence of PI in non-device cardiac surgery patients. This is an interesting finding given the increased severity of disease state and overall potential risk for PI evidenced by variables such as longer operating room times, immobility times, length of stay, etc., which were discovered. In this study, the primary null hypothesis is rejected in favor of the alternative hypothesis as age, mechanical ventilation time and preoperative Braden Risk Assessment score were determined to be significant predictors of pressure injury in the VAD-TAH population. The secondary null hypothesis is accepted as there were no differences found in the development of PI between TAH and VAD device types. Finally, the third null hypothesis was accepted as the study did not identify any association between preoperative diagnosis of depression or anxiety on pressure injury development. However, the limitation of retrospective review and potential contribution of depression and anxiety on pressure injury risk would be better investigated with prospective studies that gauge the severity of the conditions as potential predictors to PI. A prospective study to further investigate significant risk factors, end organ perfusion and identify potential preventive mechanisms that decreased PI incidence in this population is warranted.

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References

Abed, M. A., Kloub, M. I., & Moser, D. K. (2014). Anxiety and adverse health outcomes among cardiac patients: A biobehavioral model. *The Journal of Cardiovascular Nursing*, *29*(4), 354–363. https://doi.org/10.1097/JCN.0b013e318292b235

Aissaoui, N., Jouan, J., Gourjault, M., Diebold, B., Ortuno, S., Hamdan, A., … Morshuis, M. (2018). Understanding Left Ventricular Assist Devices. *Blood Purification*, *46*(4), 292–300. https://doi.org/10.1159/000491872

Allen, L. A., Smoyer Tomic, K. E., Wilson, K. L., Smith, D. M., & Agodoa, I. (2013). The inpatient experience and predictors of length of stay for patients hospitalized with systolic heart failure: Comparison by commercial, Medicaid, and Medicare payer type. *Journal of Medical Economics*, *16*(1), 43–54. https://doi.org/10.3111/13696998.2012.726932

Bhargava, A., Chanmugam, A., & Herman, C. (2014). Heat transfer model for deep tissue injury: A step towards an early thermographic diagnostic capability. *Diagnostic Pathology*, *9*, 36. https://doi.org/10.1186/1746-1596-9-36

Braden, B., & Bergstrom, N. (1987). A conceptual schema for the study of the etiology of pressure sores. *Rehabilitation Nursing: The Official Journal of the Association of Rehabilitation Nurses*, *12*(1), 8–12.

Braden, B. J. (1998). The relationship between stress and pressure sore formation. *Ostomy/Wound Management*, *44*(3A Suppl), 26S-36S; discussion 37S.

Brindle C.T. (2019). Prevalence, Incidence and Predictor Variables of Pressure Injuries in Patients Undergoing Ventricular Assist Device and Total Artificial Heart Surgeries: A PRISMA Systematic Review. *Dissertation Manuscript, Unpublished data.*

Brindle, C. T. (2013). Turning and repositioning the critically ill patient with hemodynamic instability. *Journal of Wound, Ostomy, and Continence Nursing: Official Publication of The Wound, Ostomy and Continence Nurses Society / WOCN*, *40*(5), 458. https://doi.org/10.1097/WON.0b013e3182a430c8

Coleman, S., Gorecki, C., Nelson, E. A., Closs, S. J., Defloor, T., Halfens, R., … Nixon, J. (2013). Patient risk factors for pressure ulcer development: Systematic review. *International Journal of Nursing Studies*, *50*(7), 974–1003. https://doi.org/10.1016/j.ijnurstu.2012.11.019

Coleman, S., Nixon, J., Keen, J., Wilson, L., McGinnis, E., Dealey, C., … Nelson, E. A. (2014). A new pressure ulcer conceptual framework. *Journal of Advanced Nursing*, *70*(10), 2222–2234. https://doi.org/10.1111/jan.12405

www.manaraa.com

Cooper, D. N., Jones, S. L., & Currie, L. A. (2015). Against All Odds: Preventing Pressure Ulcers in High-Risk Cardiac Surgery Patients. *Critical Care Nurse*, *35*(5), 76–82. https://doi.org/10.4037/ccn2015434

Cotts, W. G., McGee, E. C., Myers, S. L., Naftel, D. C., Young, J. B., Kirklin, J. K., & Grady, K. L. (2014). Predictors of hospital length of stay after implantation of a left ventricular assist device: An analysis of the INTERMACS registry. *The Journal of Heart and Lung Transplantation*, *33*(7), 682–688. https://doi.org/10.1016/j.healun.2014.02.022

Defloor, T. (1999). The risk of pressure sores: A conceptual scheme. *Journal of Clinical Nursing*, *8*(2), 206–216.

Doering, L. V., Moser, D. K., Lemankiewicz, W., Luper, C., & Khan, S. (2005). Depression, healing, and recovery from coronary artery bypass surgery. *American Journal of Critical Care: An Official Publication, American Association of Critical-Care Nurses*, *14*(4), 316–324.

Dripps, R. D., Lamont, A., & Eckenhoff, J. E. (1961). The role of anesthesia in surgical mortality. *JAMA*, *178*, 261–266.

Edsberg, L. E., Black, J. M., Goldberg, M., McNichol, L., Moore, L., & Sieggreen, M. (2016). Revised National Pressure Ulcer Advisory Panel Pressure Injury Staging System: Revised Pressure Injury Staging System. *Journal of Wound, Ostomy, and Continence Nursing: Official Publication of The Wound, Ostomy and Continence Nurses Society*, *43*(6), 585–597. https://doi.org/10.1097/WON.0000000000000281

El Banayosy, A., Kizner, L., Arusoglu, L., Morshuis, M., Brehm, C., Koerfer, R., … Slepian, M. J. (2014). Home Discharge and Out-of-Hospital Follow-Up of Total Artificial Heart Patients Supported by a Portable Driver System. *Asaio Journal*, *60*(2), 148–153. https://doi.org/10.1097/MAT.0000000000000046

Estep, J. D., Starling, R. C., Horstmanshof, D. A., Milano, C. A., Selzman, C. H., Shah, K. B., … ROADMAP Study Investigators. (2015). Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients: Results From the ROADMAP Study. *Journal of the American College of Cardiology*, *66*(16), 1747–1761. https://doi.org/10.1016/j.jacc.2015.07.075

Ettema, R. G. A., Van Koeven, H., Peelen, L. M., Kalkman, C. J., & Schuurmans, M. J. (2014). Preadmission interventions to prevent postoperative complications in older cardiac surgery patients: a systematic review. *International Journal of Nursing Studies*, *51*, 251–260. https://doi.org/10.1016/j.ijnurstu.2013.05.011

Feuchtinger, J., Halfens, R. J. G., & Dassen, T. (2005). Pressure ulcer risk factors in cardiac surgery: A review of the research literature. *Heart & Lung: The Journal of Critical Care*, *34*(6), 375–385. https://doi.org/10.1016/j.hrtlng.2005.04.004

www.manaraa.com

Feuchtinger, Johanna, Halfens, R., & Dassen, T. (2007). Pressure ulcer risk assessment immediately after cardiac surgery--does it make a difference? A comparison of three pressure ulcer risk assessment instruments within a cardiac surgery population. *Nursing in Critical Care*, *12*(1), 42–49. https://doi.org/10.1111/j.1478-5153.2006.00198.x

Fred, C., Ford, S., Wagner, D., & Vanbrackle, L. (2012). Intraoperatively acquired pressure ulcers and perioperative normothermia: A look at relationships. *AORN Journal*, *96*(3), 251–260. https://doi.org/10.1016/j.aorn.2012.06.014

Gefen, A., Farid, K. J., & Shaywitz, I. (2013). A review of deep tissue injury development, detection, and prevention: Shear savvy. *Ostomy/Wound Management*, *59*(2), 26–35.

Gefen, A., van Nierop, B., Bader, D. L., & Oomens, C. W. (2008). Strain-time cell-death threshold for skeletal muscle in a tissue-engineered model system for deep tissue injury. *Journal of Biomechanics*, *41*(9), 2003–2012. https://doi.org/10.1016/j.jbiomech.2008.03.039

Haesler, E. (2014). *National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, Pan Pacific Pressure Injury Alliance: Guidelines for the Prevention and Treatment of Pressure Ulcers.* Perth, Australia.

Huffman, J. C., Celano, C. M., & Januzzi, J. L. (2010). The relationship between depression, anxiety, and cardiovascular outcomes in patients with acute coronary syndromes. *Neuropsychiatric Disease and Treatment*, *6*, 123–136.

Kang, Z.-Q., & Zhai, X.-J. (2015). The Association between Pre-existing Diabetes Mellitus and Pressure Ulcers in Patients Following Surgery: A Meta-analysis. *Scientific Reports*, *5*, 13007. https://doi.org/10.1038/srep13007

Kirisci, M., Oktar, G. L., Ozogul, C., Oyar, E. O., Akyol, S. N., Demirtas, C. Y., & Arslan, M. (2013). Effects of adrenomedullin and vascular endothelial growth factor on ischemia/reperfusion injury in skeletal muscle in rats. *The Journal of Surgical Research*, *185*(1), 56–63. https://doi.org/10.1016/j.jss.2013.05.053

Krause, J. S., & Broderick, L. (2004). Patterns of recurrent pressure ulcers after spinal cord injury: Identification of risk and protective factors 5 or more years after onset. *Archives of Physical Medicine and Rehabilitation*, *85*(8), 1257–1264. https://doi.org/10.1016/j.apmr.2003.08.108

Krueger, H., Noonan, V. K., Williams, D., Trenaman, L. M., & Rivers, C. S. (2013). The influence of depression on physical complications in spinal cord injury: Behavioral mechanisms and health-care implications. *Spinal Cord*, *51*(4), 260–266. https://doi.org/10.1038/sc.2013.3

Lance, C., & Vandenberg, R. (2009). *Statistical and Mythological Myths and Urban Legends: Doctrine, Verity and Fable in the Organizational and Social Sciences.* New York: Routledge Taylor & Francis Group.

www.manaraa.com

Li, Y., Glance, L. G., Cai, X., & Mukamel, D. B. (2008). Adverse hospital events for mentally ill patients undergoing coronary artery bypass surgery. *Health Services Research*, *43*(6), 2239–2252. https://doi.org/10.1111/j.1475-6773.2008.00875.x

Liu, P., He, W., & Chen, H.-L. (2012). Diabetes mellitus as a risk factor for surgery-related pressure ulcers: A meta-analysis. *Journal of Wound, Ostomy, and Continence Nursing: Official Publication of The Wound, Ostomy and Continence Nurses Society*, *39*(5), 495–499. https://doi.org/10.1097/WON.0b013e318265222a

Munro CA. (2010). The development of a pressure ulcer risk-assessment scale for perioperative patients. *AORN Journal*, *92*(3), 272–287. https://doi.org/10.1016/j.aorn.2009.09.035

O'Brien, D. D., Shanks, A. M., Talsma, A., Brenner, P. S., & Ramachandran, S. K. (2014). Intraoperative risk factors associated with postoperative pressure ulcers in critically ill patients: A retrospective observational study. *Critical Care Medicine*, *42*(1), 40–47. https://doi.org/10.1097/CCM.0b013e318298a849

Oomens, C. W. J., Loerakker, S., & Bader, D. L. (2010). The importance of internal strain as opposed to interface pressure in the prevention of pressure related deep tissue injury. *Journal of Tissue Viability*, *19*(2), 35–42. https://doi.org/10.1016/j.jtv.2009.11.002

Oomens, Cees W. J., Bader, D. L., Loerakker, S., & Baaijens, F. (2015). Pressure induced deep tissue injury explained. *Annals of Biomedical Engineering*, *43*(2), 297–305. https://doi.org/10.1007/s10439-014-1202-6

Padula, W. V., & Delarmente, B. A. (2019). The national cost of hospital-acquired pressure injuries in the United States. *International Wound Journal*, *16*(3), 634–640. https://doi.org/10.1111/iwj.13071

Prevention of Perioperative Pressure Injury Tool Kit - AORN. (n.d.). Retrieved June 25, 2019, from https://www.aorn.org/guidelines/clinical-resources/tool-kits/prevention-of-perioperative-pressure-injury-tool-kit

Puntel, G. O., Carvalho, N. R., Dobrachinski, F., Salgueiro, A. C. F., Puntel, R. L., Folmer, V., … Soares, F. A. A. (2013). Cryotherapy reduces skeletal muscle damage after ischemia/reperfusion in rats. *Journal of Anatomy*, *222*(2), 223–230. https://doi.org/10.1111/joa.12009

Rao, A. D., Preston, A. M., Strauss, R., Stamm, R., & Zalman, D. C. (2016). Risk Factors Associated With Pressure Ulcer Formation in Critically Ill Cardiac Surgery Patients: A Systematic Review. *Journal of Wound, Ostomy, and Continence Nursing: Official Publication of The Wound, Ostomy and Continence Nurses Society / WOCN*, *43*(3), 242–247. https://doi.org/10.1097/WON.0000000000000224

Repetto, M., Semprine, J., & Boveris, A. (2012). Lipid Peroxidation: Chemical Mechanism, Biological Implications and Analytical Determination. In A. Catala (Ed.), *Lipid Peroxidation*. Retrieved from http://www.intechopen.com/books/lipid-peroxidation/lipid-peroxidation-chemical-mechanism-biological-implications-and-analytical-determination

www.manaraa.com

Reynard, A. K., Butler, R. S., McKee, M. G., Starling, R. C., & Gorodeski, E. Z. (2014). Frequency of depression and anxiety before and after insertion of a continuous flow left ventricular assist device. *The American Journal of Cardiology*, *114*(3), 433–440. https://doi.org/10.1016/j.amjcard.2014.05.015

Schuurman, J.-P., Schoonhoven, L., Keller, B. P. J. A., & van Ramshorst, B. (2009). Do pressure ulcers influence length of hospital stay in surgical cardiothoracic patients? A prospective evaluation. *Journal of Clinical Nursing*, *18*(17), 2456–2463. https://doi.org/10.1111/j.1365-2702.2008.02711.x

Shapiro, P. A., Levin, H. R., & Oz, M. C. (1996). Left ventricular assist devices. Psychosocial burden and implications for heart transplant programs. *General Hospital Psychiatry*, *18*(6 Suppl), 30S-35S.

Silva Enciso, J. (2016). Mechanical Circulatory Support: Current Status and Future Directions. *Progress in Cardiovascular Diseases*, *58*(4), 444–454. https://doi.org/10.1016/j.pcad.2016.01.006

Snipelisky, D., Stulak, J. M., Schettle, S. D., Sharma, S., Kushwaha, S. S., & Dunlay, S. M. (2015). Psychosocial characteristics and outcomes in patients with left ventricular assist device implanted as destination therapy. *American Heart Journal*, *170*(5), 887–894. https://doi.org/10.1016/j.ahj.2015.08.012

Sprigle, S., & Sonenblum, S. (2019). Visualizing Tissue Strain Under the Sacrum and Coccyx in Different Supine Postures: A Case Series. *Advances in Skin & Wound Care*, *32*(6), 264–271. https://doi.org/10.1097/01.ASW.0000554445.59743.44

The Joint Commission. (2008). Strategies for Preventing Pressure Ulcers. *Joint Commission Perspectives on Patient Safety*, *8*(1), 5–7.

Vangilder, C., Macfarlane, G. D., & Meyer, S. (2008). Results of nine international pressure ulcer prevalence surveys: 1989 to 2005. *Ostomy/Wound Management*, *54*(2), 40–54.

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Concluding Narrative

The dissertation research described herein discussed the investigation of PI incidence, risk factors and predictor variables for the development of pressure injuries in cardiac surgery patients undergoing VAD-TAH surgeries. A systematic review using PRISMA methodology was unable to identify any articles which described the reported incidence, prevalence or risk factors for the VAD-TAH surgical population. Because of this, a review of a surrogate population including the on-pump CABG patient served to identify potential variables of further study. The systematic review suggested: ASA score, age, diabetes mellitus, cardiac arrest, preoperative corticosteroids, BMI, OR time, cardiac disease severity, and mechanical ventilation as potential risk factors to consider. The results guided the first, 8-year retrospective analysis of VAD and TAH patients to identify incidence, and predictors of PI development in a large academic university health center in the United States.

The retrospective study identified 361 VAD-TAH cases between study years 2010-2018, with the final sample for investigation including 292 independent VAD-TAH surgical cases conducted in 265 patients. In total, 32 patients developed 45 pressure ulcers. Despite some subjects having multiple surgical admissions during the study period, all pressure ulcers developed in individual patients during a single admission. The incidence of PI per all surgical cases was 11% (32/292), with PI incidence per patient of 12% (32/265). Incidence density was found to be (10/1000) 1% for 2010-2012, (12/1000) 1.2% for 2013-2015, and (10/920) 1.1% for 2016-2018 respectively. Mean hospital length of stay by device included 34.8 days for HVAD, 43.5 for HM2, 35.5 for HM3 and 108.6 days for TAH. The overall incidence of pressure injury in this study was much lower than anticipated given historical incidence of PI in

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non-device cardiac surgery patients. This is an interesting finding given the increased severity of disease state and overall potential risk for PI evidenced by variables such as longer operating room times, immobility times, length of stay, etc., which were discovered. In this study, the primary null hypothesis is rejected in favor of the alternative hypothesis as age, mechanical ventilation time and preoperative Braden Risk Assessment score were determined to be significant predictors of pressure injury in the VAD-TAH population. The secondary null hypothesis is accepted as there were no differences found in the development of PI between TAH and VAD device types. Finally, the third null hypothesis was accepted as the study did not identify any association between preoperative diagnosis of depression or anxiety on pressure injury development. However, the limitation of retrospective review and potential contribution of depression and anxiety on pressure injury risk would be better investigated with prospective studies that gauge the severity of the conditions as potential predictors to PI.

Given the outcomes of the systematic review which was not able to identify any existing research in VAD-TAH patients to guide a retrospective review, and the limitations of a retrospective review which increase the risk of accuracy via information bias and selection bias, the results of this dissertation study will inform future research.

Because the incidence of PI in VAD-TAH patients was lower than expected, future studies should focus on both a prospective investigation to more accurately define predictor variable. For example, the secondary aim will be to evaluate the effect of depression and anxiety severity on PI development and predictor variables. This builds on the dissertation study, which assessed the dichotomous preoperative medical history of depression and anxiety, while the future study will allow for prospective preoperative measurement of depression and anxiety. The generalized anxiety disorder 7-item (GAD-7) scale and the patient health questionnaire-9 (PHQ-

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9) will be used, as they are sensitive tools for the preoperative setting, are valid and reliable in the cardiac population and may predict cardiac mortality (Abed, Kloub, & Moser, 2014; Reynard et al., 2014). The hypothesis is that patients who develop PI will have statistically significant elevations in oxidative stress biomarkers compared to patients who do not develop PI; and statistically significant differences in anxiety and depression severity scores will be associated with levels of oxidative stress biomarkers and PI occurrence. In addition, exploring potential mitigating factors that led to lower than anticipated incidence in the retrospective study could focus on to what extent is the postoperative cardiac output of TAH-VAD patients influences PI prevention versus development? Although VAD-TAH patients have high preoperative comorbid status, implantable ventricular devices may substantially improve baseline cardiac output, leading to improved oxygenation, perfusion and less oxidative stress. Additionally, the PI prevention culture of the facility where the patients received care demonstrated a preoperative to postoperative continuum of preventive care which may have had a significant impact on the low incidence density that was reported over the eight-year study.

Future Program of Research

Baseline Oxidative Stress Feasibility Study

As described in the conceptual framework, oxidative stress plays a major role in the pathophysiology of PI development. A proposed program of research would be a prospective, longitudinal observational feasibility study to investigate the natural history of oxidative stress profiles in VAD-TAH population. The primary aim will be to explore oxidative stress biomarkers of operating room acquired PI in adult VAD-TAH patients at VCU to determine feasibility for a larger study. The research will investigate biomarkers of oxidative stress by evaluating lipidomic markers in serum (levels of F_2-Isoprostane) and urine (levels of 2,3, dinor-

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15- F_2-Isoprostane and 5,6,dihydro-15- F_2-Isoprostane metabolites), which are established markers of oxidative stress (Milne et al., 2015; Morrow, Awad, Kato, et al., 1992; Morrow et al., 1990; Morrow, Awad, Boss, et al., 1992).

For this study, patients will be approached in the pre-surgical clinic visit or perioperative unit for informed consent, baseline serum and urine samples for biomarker analysis, and completion of the GAD-7, PHQ-9 and demographics forms. Graduate assistants will be utilized to assist with patient enrollment and to transport laboratory samples. For longitudinal analysis of biomarkers, nine serum and urine samples will be collected using established guidelines and protocols from invasive lines and the Foley catheter respectively at longitudinal time points as described in figure 2 (Chiu, Wang, & Blumenthal, 1976; Halliwell & Lee, 2010; Il'yasova, Morrow, Ivanova, & Wagenknecht, 2004; Seet et al., 2011). Gas chromatography-mass spectrometry will be used to analyze urine and serum biomarkers under the guidance of the mass spectrometry core facility with expertise in biochemical-lipidomic analysis (Milne, Gao, Terry, Zackert, & Sanchez, 2013). In summary, the second study would seek to understand what the baseline levels of lipid biomarkers to oxidative stress are in the VAD-TAH patient and describe any differences between those levels in patients with or without PI and any correlation with preoperative anxiety and depression scores. This study would be foundational in its description of serum and urine biomarker levels in this population and based on the findings, direct the aims of the third study.

Follow-Up Oxidative Stress Study

The third study can enhance and expand the aims in the oxidative stress feasibility study while allowing for potential new discoveries. The proposed third study will be a larger biomarker study that builds upon findings from the second study. In the lipidomic mass spectrometry

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analysis of oxidative stress biomarkers, it is anticipated that significant elevations in F2-isoprostanes and/or associated metabolites from PI during VAD-TAH intervention will be seen. The purpose of the second study would be to evaluate and quantify levels of these metabolites that are most closely associated with PI and explore alternate approaches for biomarker evaluation. In addition to blood serum and urine samples, for example, methods for collecting and analyzing exhaled breath for levels of these metabolites have proven to be highly reliable, accurate and feasible (Janicka, Kubica, Kot-Wasik, Kot, & Namieśnik, 2012).

In the event the second study failed to identify any connection between PI incidence and levels of isoprostanes, the third study may repeat study two by evaluating evidence of mitochondrial IR. Intracellular mitochondrial approximation to elevated oxidant molecules such as ROS superoxides have been linked to apoptosis in animal models of skeletal IR (Tran, Tu, Liu, Muelleman, & Li, 2012). This could be evaluated by looking at levels of cardiolipin peroxidation which is directly associated with mitochondrial IR (Shen, Ye, McCain, & Greenberg, 2015). This would allow the current conceptual model to remain without change except for altering the oxidant metabolite of IR studied.

In summary, the goal of this developing program of research was to first describe the incidence and predictor variables of PI in the VAD-TAH population. From this starting point, progressive studies will further explore the role of PI formation as it relates to the potential physiologic response of the tissue and cells to IR injury following surgery through the identification of biomarkers associated with PI injury as it relates to oxidative stress. Such biomarkers provide potential diagnostic markers of PI injury and could be further developed as a point of care diagnostic. Clinically, this would provide a great benefit by providing an objective

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biomarker versus the current standard of care, visual skin assessments, which do not adequately reflect damage occurring in the muscle tissue.

References

Abed, M. A., Kloub, M. I., & Moser, D. K. (2014). Anxiety and adverse health outcomes among cardiac patients: a biobehavioral model. *The Journal of Cardiovascular Nursing*, *29*, 354–363. https://doi.org/10.1097/JCN.0b013e318292b235

Chiu, D., Wang, H. H., & Blumenthal, M. R. (1976). Creatine phosphokinase release as a measure of tourniquet effect on skeletal muscle. *Archives of Surgery*, *111*, 71–74.

Halliwell, B., & Lee, C. Y. J. (2010). Using isoprostanes as biomarkers of oxidative stress: some rarely considered issues. *Antioxidants & Redox Signaling*, *1*3, 145–156. https://doi.org/10.1089/ars.2009.2934

Il'yasova, D., Morrow, J. D., Ivanova, A., & Wagenknecht, L. E. (2004). Epidemiological marker for oxidant status: comparison of the ELISA and the gas chromatography/mass spectrometry assay for urine 2,3-dinor-5,6-dihydro-15-F2t-isoprostane. *Annals of Epidemiology*, *14*, 793–797. https://doi.org/10.1016/j.annepidem.2004.03.003

Janicka, M., Kubica, P., Kot-Wasik, A., Kot, J., & Namieśnik, J. (2012). Sensitive determination of isoprostanes in exhaled breath condensate samples with use of liquid chromatography-tandem mass spectrometry. *Journal of Chromatography. B, Analytical Technologies in the Biomedical and Life Sciences*, *893-894*, 144–149. https://doi.org/10.1016/j.jchromb.2012.03.005

Milne, G. L., Dai, Q., & Roberts, L. J. (2015). The isoprostanes--25 years later. *Biochimica Et Biophysica Acta*, *1851*, 433–445. https://doi.org/10.1016/j.bbalip.2014.10.007

Milne, G. L., Gao, B., Terry, E. S., Zackert, W. E., & Sanchez, S. C. (2013). Measurement of F2-isoprostanes and isofurans using gas chromatography-mass spectrometry. *Free Radical Biology & Medicine*, *59*, 36–44. https://doi.org/10.1016/j.freeradbiomed.2012.09.030

Morrow, J. D., Awad, J. A., Boss, H. J., Blair, I. A., & Roberts, L. J. (1992). Non-cyclooxygenase-derived prostanoids (F2-isoprostanes) are formed in situ on phospholipids. *Proceedings of the National Academy of Sciences of the United States of America*, *89*, 10721–10725.

Morrow, J. D., Awad, J. A., Kato, T., Takahashi, K., Badr, K. F., Roberts, L. J., & Burk, R. F. (1992). Formation of novel non-cyclooxygenase-derived prostanoids (F2-isoprostanes) in carbon tetrachloride hepatotoxicity. An animal model of lipid peroxidation. *The Journal of Clinical Investigation*, *90*, 2502–2507. https://doi.org/10.1172/JCI116143

Morrow, J. D., Hill, K. E., Burk, R. F., Nammour, T. M., Badr, K. F., & Roberts, L. J. (1990). A series of prostaglandin F2-like compounds are produced in vivo in humans by a non-

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cyclooxygenase, free radical-catalyzed mechanism. *Proceedings of the National Academy of Sciences of the United States of America*, *87*, 9383–9387.

Reynard, A. K., Butler, R. S., McKee, M. G., Starling, R. C., & Gorodeski, E. Z. (2014). Frequency of depression and anxiety before and after insertion of a continuous flow left ventricular assist device. *The American Journal of Cardiology*, *114*, 433–440. https://doi.org/10.1016/j.amjcard.2014.05.015

Seet, R. C. S., Lee, C.-Y. J., Loke, W. M., Huang, S. H., Huang, H., Looi, W. F., … Halliwell, B. (2011). Biomarkers of oxidative damage in cigarette smokers: which biomarkers might reflect acute versus chronic oxidative stress? *Free Radical Biology & Medicine*, *50*, 1787–1793. https://doi.org/10.1016/j.freeradbiomed.2011.03.019

Shen, Z., Ye, C., McCain, K., & Greenberg, M. L. (2015). The Role of Cardiolipin in Cardiovascular Health. *BioMed Research International*, *2015*, 891707. https://doi.org/10.1155/2015/891707

Tran, T. P., Tu, H., Liu, J., Muelleman, R. L., & Li, Y.-L. (2012). Mitochondria-derived superoxide links to tourniquet-induced apoptosis in mouse skeletal muscle. *PloS One*, *7*, e43410. https://doi.org/10.1371/journal.pone.0043410

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Vita

Christopher Tod Brindle was born on April 23, 1978, in Tallahassee, Florida and is an American citizen. He graduated from Brooke Point High School, Stafford, Virginia in 1996. He received his Bachelor of Science in Nursing degree in 2001 from THE Ohio State University and a post-Baccalaureate education in Enterostomal Therapy from the Cleveland Clinic, with board certification as a Wound Ostomy Continence Nurse. He received his Master of Science in Nursing Administration and Leadership from the Virginia Commonwealth University in 2011. He started his nursing career working at the James Cancer Hospital and Solove Research Institute at THE Ohio State University Medical Center from 2001-2004, was a travel-nurse working in Arizona, Ohio and Virginia from 2004-2006 and served on the VCU wound care team from 2006-2017 as the clinical coordinator. During this time, he served on the Board of Directors for the Association for the Advancement of Wound Care, the National Conference Planning Committee for the Wound Ostomy Continence Nurses Society, was named an Honorary Fellow of the University of Melbourne School of Medicine, Dentistry and Health Sciences 2017-2019. He served on the American Nursing Credentialing Center (ANCC) Magnet Commission for three years and held an editorial position on the Journal of Tissue Regeneration and Healing. Tod has presented over 200 international presentations, authored 5 book chapters and over 40 peer reviewed journals and scientific posters. Additionally, he has been humbled to receive over 15 awards for clinical practice, including the prestigious ANCC Magnet National Nurse of the Year 2013, the Ohio State College of Nursing Centennial Award for the top 100 Alumni Transformers in Nursing and Healthcare 2014, Distinguished Alumnus Award from THE Ohio State and the Virginia Nurses Foundation Magnet Consortium Award for Excellence in Clinical Practice. After briefly acting as the Chief Clinical Officer for a startup company from 2017-2018, he acted as the Global Clinical Director for Mölnlycke Healthcare 2018-2019, Gothenburg, Sweden and was recently asked to serve as the United States Medical Director for Mölnlycke Healthcare in Norcross, GA.

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