Venous Thromboembolism in Patients with Thermal Injury

A Review of Risk Assessment Tools and Current Knowledge on the Effectiveness and Risks of Mechanical and Chemical Prophylaxis

Christopher J. Pannucci, MD, MS[a,*], Andrea T. Obi, MD[b], Benjamin H. Timmins, MD[c], Amalia L. Cochran, MD, MA[d]

KEYWORDS

• Deep venous thrombosis • Pulmonary embolus • VTE prophylaxis

KEY POINTS

- Venous thromboembolism is an important patient safety issue in patients with thermal injury.
- Large database research is an excellent way to research rare events.
- Further research into the optimal means to provide chemical prophylaxis to burn patients is needed.

INTRODUCTION

Virchow's triad of stasis, hypercoagulability, and intimal damage describes the broad categories of factors that contribute to thrombotic risk. Patients with thermal injury seem to have the ideal physiologic predisposition to the Virchow's triad, and thus should be at high risk for postinjury venous thromboembolism events. Endothelial dysfunction via disruption of junctional proteins and stress fibers results in altered paracellular flow of solutes or capillary leak, manifested by edema and altered fluid balance.[1,2] Alterations in coagulation, including deficiency of natural anticoagulant antithrombin and altered fibrinogen, predispose toward a prothrombotic state.[3–6] In addition, burn dressings and use of split-thickness skin grafts make immobilization and resulting venous stasis inevitable in the current treatment paradigm of major cutaneous burns.

Virchow's triad notwithstanding, venous thromboembolism (VTE) is a rare event (0.6%) in the burn population. However, more than 10-fold variability in postinjury VTE risk exists among the overall population with thermal injury.[7,8] As a rare event, VTE in thermally injured patients cannot rigorously be studied using case series or small, single-center studies. This article reviews the current knowledge of VTE in the thermally injured populations, with a focus on (1) the utility of large-database approaches for VTE research, and (2) an overview of VTE risk stratification and prevention.

[a] Division of Plastic Surgery, University of Utah, 30 North 1900 East 3B400, Salt Lake City, UT 84132, USA; [b] Department of Surgery, University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48109, USA; [c] Division of Plastic Surgery, Oregon Health Sciences University, 3181 Southwest Sam Jackson Park Road, Portland, OR 97239, USA; [d] Department of Surgery, University of Utah Burn Center, University of Utah, 30 North 1900 East 3B400, Salt Lake City, UT 84132, USA
* Corresponding author.
E-mail address: christopher.pannucci@hsc.utah.edu

Clin Plastic Surg 44 (2017) 573–581
http://dx.doi.org/10.1016/j.cps.2017.02.002

LARGE-DATABASE APPROACHES TO RISK MODELING

Large-Database Research in Plastic Surgery, with a Focus on Rare Events

In outcomes analysis of dichotomous events (such as a yes/no VTE event), statistical analysis can examine observed differences in event frequency between patients with or without a certain risk factor, or with or without a certain intervention. Sample size calculation for dichotomous outcomes are based on the study's tolerance for type I (alpha) and type II (beta) errors, as well as the expected event rate in the two groups. Large-database research is ideally suited for outcome events that occur infrequently, or for more common outcome events in which the expected difference between 2 interventions is small. Large-database approaches allow the use of regression-based techniques to control for identified confounding variables. This method, in turn, allows more rigorous estimation of risk directly attributable to different factors. Regression is a powerful tool when used correctly but admittedly requires a high number of outcome events. In general, the so-called "rule of 10s" states that, for each additional degree of freedom in the model, 10 outcome events are required. Thus, for a regression model that contains 10 dichotomous independent variables, approximately 100 outcomes events would need to be present in the data set in order for the regression to be valid. The advantage of large-database research for rare events becomes immediately apparent here.

Large-database approaches have been used in the plastic surgery literature to examine many rare but important complications, and to examine small but important differences between two treatment modalities. Examples include use of the National Surgical Quality Improvement Program (NSQIP)[9] and the Tracking Operations and Outcomes in Plastic Surgery[10] databases to examine complications associated with acellular dermal matrix in breast reconstruction, the NSQIP to examine readmission rates after reconstructive surgery,[11,12] Medicare data to examine practice patterns in rheumatoid hand surgery,[13] and the State Inpatient Database of New York to examine the effect of Medicaid expansion on access to reconstructive breast surgery.[14] Several large-database approaches toward VTE risk model generation in surgical patients have been developed using the Veterans' Affairs Patient Safety Study,[15] the NSQIP,[16] and the Michigan Surgical Quality Collaborative,[17] although none are specific to patients with thermal injury. The authors have previously used the American Burn Association's National Burn Repository (NBR) to create a condition-specific VTE risk assessment model for thermally injured patients, as discussed later.

Universal Risk Calculators Versus Condition-Specific Risk Calculators

Bilimoria and colleagues[18] published a universal risk calculator based on more than 1 million cases in the NSQIP. This model uses a 21-point, Web-based, behind-the-scenes calculator to conceptualize and quantify risk for perioperative 30-day morbidity, 30-day mortality, and 6 additional postoperative complications. Their analysis showed that prediction for the universal calculator was similar to condition-specific models. The model was validated in a large cohort of colon surgery patients, in which the universal model and the colon-specific model performed similarly.[18]

The advantage of such a universal risk calculator is that the maximum amount of information can be obtained from a minimum amount of effort. However, this assumes that risk calculation is being performed by a person. As the interface between medicine and technology continues to improve, risk calculators will likely be run behind the scenes by computers, instead of calculated by hand by individual providers. Our prior research has shown that a computer-based VTE risk score calculation, based on administrative data, is more accurate than a physician-reported VTE risk score.[19] In this regard, it is noteworthy that, for examined complications in the study by Bilimoria and colleagues[18] (including mortality, morbidity, pneumonia, cardiac, surgical site infection, urinary tract infection, VTE, and renal failure), the colon-specific model c-statistics were slightly higher and the Brier score slightly lower. These data indicate that the procedure-specific risk assessment tool may have slightly improved calibration and discrimination compared with the universal calculator. VTE risk stratification may evolve to a behind-the-scenes calculation, and, if calculations are being performed behind the scenes by computers (eg, with no additional human effort), then the most accurate model should be used. In this regard, the authors support ongoing development of procedure-specific or injury-specific VTE risk models, if their ability to risk-stratify exceeds that of a universal calculator.

VENOUS THROMBOEMBOLISM INCIDENCE AND RISK FACTORS IN PATIENTS WITH BURNS

Incidence

Single-center studies have a reported VTE incidence as low as 0.25% when only clinically symptomatic VTE is considered, and as high as 23.3%