ABSTRACT

Objectives. The expected rate of deep vein thrombosis (DVT) after laparotomy or major joint surgery has been reported to be 20 to 50% for unprophylaxed non-native patients. DVT prophylaxis for surgical patients at the Alaska native Medical Center has typically not been offered as the perceived rate of DVT and pulmonary embolism in our patient population has been very low. Retrospective analysis of positive venous duplex scans at our institution revealed only four cases of post-operative DVT during a two-year interval. This study was designed to document the actual rate of post-operative DVT in Alaskan natives not provided with routine DVT prophylaxis.

Study Design. Prospective cohort study of DVT in open abdominal, open knee, open hip and pelvic fracture surgery patients at the Alaska native Medical Center from 1999 – 2001.

Methods. The day prior to expected discharge, we performed venous duplex ultrasonography on 67 patients with open abdominal surgery, major open knee or hip surgery, or pelvic fracture who received no DVT prophylaxis. Some patients included in the study were also asked questions about their consumption of marine mammals and fish, and the native blood quanta was estimated in all patients using existing data bases.

Results. Sixty percent of the study population was determined to be at high risk for DVT using standard risk stratification methods. Dietary habits varied widely, but were largely reported as being "traditionally" native. Nearly all patients had 50% or more "native blood". Only one of 67 patients developed a documented post-operative DVT.

Conclusions. Post-operative deep vein thrombosis in Alaskan natives not provided with routine DVT prophylaxis is rare. The data does not provide a clear indication as to why Alaskan natives may be at decreased risk for post-operative DVT.

Key Words: deep vein thrombosis, post-operative, Alaskan native, native American, chemo-prevention, prophylaxis
INTRODUCTION

Deep vein thrombosis and pulmonary embolism remain daunting problems for surgeons. Although the clinical sequelae of deep vein thrombosis are uncommon with modern methods of prophylaxis (1), the risk and cost incurred from the provision of chemo-prevention is enormous (2). Asymptomatic post-operative DVT, however, is common (1). Using sensitive methods of detection, such as the fibrinogen uptake test (FUT), meta-analysis yields expected rates of 27% for unprophylaxed patients undergoing general surgery. With heparin prophylaxis, this rate is lower (9.6%), but still striking (3). Other methods of detection such as venography, impedance plethysmography, and venous ultrasonography are also available, but, due to its availability and safety, ultrasonography emerges as the most common method of screening for post-operative DVT (4-6). The sensitivity of ultrasonography is far from perfect. By meta-analysis, level 1 studies yield a sensitivity of 62% and level 2 studies 95% (7). Even with these limitations, one would expect a rate of DVT on the order of 15 to 20% when screening post-operative patients not provided prophylaxis with venous ultrasonography.

The observed rate of DVT at the Alaska native Medical Center has always seemed low. Consequently, providing anticoagulants or sequential compression devices for our general, gynecology and orthopedic surgery patients has not been standard practice. Theories as to why this patient population might have a low rate of clinical DVT generally stem from the unique genetic traits and dietary habits of the patients attending our facility. With the exceptions of some rare, local, non-native trauma patients and a few commissioned officers in the U.S. Public Health Service, all patients seen at the 150-bed Alaska native Medical Center are documented Alaska natives or American indians. Most are eskimo or indian from interior Alaska with smaller numbers from south-east Alaska and tribes from the “lower 48” states. Bloodlines in Alaskan natives are mixed to various degrees, depending upon the region of origin. Some “full-blooded” natives from the southern part of the state have geniologies which trace back to Russian immigrants, long before western Europeans occupied the region. To date, however, no sub-population has been regarded as being “at risk” for post-operative DVT except for our small non-native cohort, for whom prophylaxis is standard.
In an attempt to approximate the frequency of post-operative DVT at our facility, all positive veinous duplex ultrasound exams performed between January 1997 and December 1998 were retrospectively reviewed. There were only four documented cases of post-operative DVT during this two-year interval. There were 4638 general surgery and orthopedic operative cases performed during this same interval, and prophylaxis for DVT was provided only on rare occasions. Based on this provocative finding, we initiated a prospective study to determine the incidence of DVT in native surgical patients who do not receive prophylaxis. Additionally, data was gathered on dietary and genetic histories in order to provide an explanation for the significantly decreased risk, if one was identified.

MATERIALS AND METHODS

Patients were selected by the operating surgeons from the departments of general and orthopedic surgery at the Alaska native Medical Center during the interval from March 1999 to July 2001. Entry criteria included major open abdominal procedures, pelvic fractures and open knee or hip surgery. Trauma and general surgery cases were eligible patients of the author, with a small contribution from three other general surgeons in the department. Patients who received anti-coagulants or sequential leg/foot compression devices (SCDs) for any reason during the peri-operative period were excluded from the study. Only one patient, deemed to be at extreme risk due to prior DVT and concurrent malignancy, was provided enoxaparin and excluded. All other patients considered for entry were enrolled. Eighty patients were recruited during the study period, including 36 from the department of general surgery and 44 from the department of orthopedics.

Patients enrolled were maintained without anti-coagulants or SCDs during the post-operative period. Recovery, rehabilitation and ambulation were per routine. Bilateral lower extremity venous duplex ultrasonography was performed on the day prior to the anticipated discharge date using an HP 2500 4.5 MHz linear transducer. Color flow, pulse doppler and compression techniques were employed. As many patients reside in remote Alaskan villages and towns, hospital follow-up was not possible. All positive venous
duplex scans performed during the study interval were cross-referenced with the database.

Patient data was collected by the physician or physician’s assistant entering the patient into the study. Parameters included for study were risk factors for DVT and dietary habits. Risk factors considered included an age of more than 60 years, history of DVT, current malignancy, obesity as defined as weighing more than 120% of ideal body weight, and a major medical illness limiting mobility. Patients were risk-stratified, according to Gallus and Salzman (8), into high, moderate and low risk categories. For 51 patients, data was available regarding perceived "traditional" and "western" dietary habits. For 19 of these patients, estimated frequencies of fish and sea mammal consumption were obtained.

Data was also collected from the existing database regarding the estimated native blood quantum. This information is routinely collected when patients or their ancestors enter the Indian Health Service system.

RESULTS

Patients
Eighty patients were enrolled into the study. Thirteen were dropped from the analysis due to laparoscopic or breast procedures (n = 11), or the provision of anti-coagulation treatment for vascular surgery (n = 2), which is standard to prevent arterial graft thrombosis. Sixty-seven patients thus met the entry criteria and remained for analysis, including 34 following general surgery/trauma and 33 after major lower extremity joint surgery. The median age of the cohort was 63 (range = 32-94) with 44 (66%) over the age of 60. There were 28 men and 39 women. No patient had a prior history of DVT. Obesity, defined as a weight >120% of the patient’s ideal body weight, was identified in 24 (37%), and 15 (22%) had an intra-abdominal malignancy at the time of surgery. Major medical illness restricting mobility was identified in 8 (14%). According to the standard DVT risk stratification (8), 40 (60%) were considered to be at "high" risk, 25 (37%) at "moderate" risk, and 2 (3%) at "low" risk for post-operative DVT.

Dietary habits were reported to be "traditional" by 39 of the 51 patients for whom data was available, the remaining 12 characteri-
zing their diet as being "western". When asked to quantify their average fish intake, 12 of 19 (63%) reported one or more meal per week containing some fish and 5 (26%) reported at least one meal per week to contain sea mammal (whale, walrus, seal, polar bear) or sea mammal products (seal oil). Upon analysis of "native blood" quanta, 43 of 65 patients (66%) were more than three-quarters, 60 (92%) were half or more, and 64 (98%) were one quarter or more. The mean "native blood" value for the group was 0.85 (7/8).

Deep vein thrombosis
One of the 67 patients, an 85-year-old woman with no other risk factors, was found to have post-operative DVT by duplex examination following hip fracture surgery. The clot was non-occlusive in the common femoral vein ipsilateral to the surgical site, with a superficial thrombus also noted in the lesser saphenous of the same leg. No other deep vein thrombi were identified in any surgical patients during the study period.

DISCUSSION
The consequences of untreated deep vein thrombosis can be devastating or fatal. In an effort to minimize significant pulmonary embolism and post-thrombotic syndrome, the provision of prophylaxis for surgical patients has become common practice and, possibly, over-emphasized (9). Many low-risk patients are provided with anti-coagulants or a compression hose for minor surgical procedures, incurring huge costs and exposing the patient to increased risks of adverse drug reaction and bleeding (10). For the high-risk patient, however, prophylaxis appears to be valuable. As the frequency of deep vein thrombosis in the absence of prophylaxis has been reported to be 16-30% for mixed general surgery and 50-70% for major knee/hip surgery and acute trauma (3, 10, 11), it would seem reasonable to provide such patients with prophylaxis. The observed frequencies of symptomatic deep vein thrombosis in similar patients at our facility have consistently been low. Consequently, it has not been standard practice to provide DVT prophylaxis for our Alaska native surgical patients.
The present study documents an exceedingly low rate of DVT (<2%) in moderate- to high-risk Alaskan native surgical patients not provided prophylaxis for DVT. The predicted incidence for the study population would be 30-60% or higher as more than half of the group fell into a high-risk category. We found only one.

Limitations of the present study include suboptimal methods of DVT detection, possible selection bias, and the limited sampling of dietary intake data. As fibrinogen uptake tests and venography are the gold standards for the detection of DVT, it is possible that some clots were overlooked as a result of using the less sensitive ultrasound screening methods. The reliability of ultrasound in this setting is uncertain. Meta-analysis of level 1 studies evaluating this issue estimates a sensitivity of 62% (7). If a sensitivity of 62% and an expected rate of DVT of 30-60% (10, 12-14) are assumed, the number of DVTs anticipated in this study would be 12 to 24. The study group may also be subject to a selection bias. Most of those enrolled were sequentially eligible patients of the author and the department of orthopaedics. However, one patient was intentionally provided anti-coagulation treatment and was therefore excluded from the study. This patient was at extreme risk for DVT and could have developed a clot. Had he been included, and in fact developed DVT, the number of positive tests might have been two, which is still well below the expected number. A majority of the remaining patients were, in fact, at high risk by standard criteria, yet their actual rate of DVT formation was well below published controls. Dietary information was limited to a small subset of patients enrolled later in the study and is of little value in the determination of a possible etiology for clot resistance in the study population. It is only presented here because it was obtained and may provide some insight for future investigation.

Demonstration of a difference in the probability of DVT between native and non-native Americans leads to a discussion regarding possible etiologies. A search of the National Library of Medicine database provides some possible explanations. A study by Gregg et al. found no factor V-Leiden mutations in a group of 54 native Americans. White Americans and white Europeans experience a 4.4% rate of such mutations, which cause resistance to activated protein C and hypercoagulability (15). A similar study by Ridker et al. found factor V-Leiden mutations in 5.3% of whites and 1.25% of the 80
native Americans tested (16). In a series of studies by Dyerberg et al., Greenland eskimos had higher levels of platelet omega-3 fatty acids, two-fold longer bleeding times, and depressed platelet aggregation when compared to a Danish group (17). If one postulates potential genotypic similarity between Asians and native Americans, a study by Iso et al. may also provide some insight. Prompted by differences between American and Japanese frequencies of stroke and coronary artery disease, their study demonstrated significantly lower fibrinogen levels in the Japanese relative to Americans (18). Activities of factors VII and VIII were also lower in the Japanese, but Japanese-American and Caucasian activities were similar. This raises the possibility of a dietary or environmental factor influencing the risk for DVT.

In the present study, limited data on self-reported dietary intake was obtained because the decision to collect this information was made late in the study period. Of the 39 study patients queried, 76% reported their diet to be "traditional". However, only 63% of 19 patients who were questioned further reported one or more meal per week with fish, and only 26% reported one or more meal per week containing some sea mammal or a sea mammal product. The mainstay of the traditional diet for most of the study group is sea mammal and fish. Berries, caribou and moose are also consumed, especially by natives living in remote villages. However, a large portion of the population that we serve no longer resides in the "bush". Census data from 2000 reveals that more than half of our typical catchment population is urbanized, living in proximity to Anchorage, and fully one-third of all Alaskan natives live in the urban area (19). Many who reside in the Anchorage area have adopted a typical American diet, supplementing the latter with traditional foods on special occasions and when available. In fact, western diets have become more popular even in remote areas, as evidenced by the current epidemics of obesity and diabetes amongst Alaskan natives living in all parts of the state. An important dietary influence therefore seems less likely, although the available data is not sufficient to draw any definite conclusions. Further evaluation of the possible impact of traditional foods is needed.

In conclusion, Alaskan natives experience post-operative deep vein thrombosis with a significantly lower frequency than that published for non-native Americans. Even without the provision of DVT
prophylaxis, the formation of lower extremity deep vein thrombi during the post-operative period for our patients is rare, as assessed by duplex ultrasonography screening. There is, as yet, no good data to explain this marked difference between Alaskan natives and published controls. Based upon limited dietary information and a few small studies of ethnic variances in clotting tendencies, a genetic factor, rather than a dietary influence, seems the more likely explanation. Further studies are needed to determine the reason for this.

Novel approaches to post-surgical DVT prophylaxis with lower complication rates may result from such research.

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