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Regular Article

Risk of deep vein thrombosis in patients with cellulitis and erysipelas ☆ A systematic review and meta-analysis

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ABSTRACT

Introduction: The occurrence of deep vein thrombosis (DVT) is often considered in patients with cellulitis and erysipelas because of the common presentation of unilateral limb swelling, erythema and pain. Different authors however have reached different conclusions about the prevalence of DVT in these patients and for the need for compression ultrasound (CUS). The purpose of this study is to determine the prevalence of DVT in patients with cellulitis and erysipelas, and inform the utility of CUS.

Methods: A systematic literature search was conducted of Medline and Cochrane for studies that reported groups of patients with cellulitis or erysipelas who had CUS to evaluate for DVT. Study quality assessment was based on the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies. The incidence rates from the included studies were pooled using a random-effects model to calculate an overall DVT rate. Individual and pooled DVT rates with corresponding upper and lower limits were graphed as a forest plot. Between-study heterogeneity was estimated using the I^2 statistic.

Results: Nine studies were included totaling 1054 patients with cellulitis or erysipelas with 18 DVTs. The overall pooled incidence rate was 2.1% (95% confidence interval, 0.5%-9.1%) for proximal DVT and 3.1% (95% confidence interval, 1.9%-4.9%) for any DVT. When analyzed separately, the pooled incidence rate for the three retrospective studies was 1.1% (95% CI, 0.6%-2.2%), while the rate for the six prospective studies was 7.8% (95% CI, 4.2%-14.2%).

Conclusion: The risk of DVT in cellulitis and erysipelas is low compared to the average risk of patients referred for CUS and comparable to low risk patients as determined by the commonly employed Wells criteria.

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Introduction

Cellulitis and erysipelas are common types of skin and soft tissue infection resulting in more than 600,000 hospitalizations per year in the United States [1]. Cellulitis is generally defined as any spreading infection involving the dermis and subcutaneous tissues [2], whereas erysipelas is a subtype of cellulitis involving the superficial dermal structures and distinguished clinically by raised borders and clear demarcation between involved and uninvolved skin [3]. The occurrence of deep vein thrombosis (DVT) is often considered in patients with these infections because of the common presentation of unilateral limb swelling, erythema and pain [4,5]. A recent prospective study from Denver for example reported that 42% of patients admitted with cellulitis received ultrasounds [6], primarily to rule out DVT (author personal communication). Other authors note that cellulitis and erysipelas are among the most common conditions in patients referred to assess for DVT [7,8], and account for up to 20% of ultrasound scans [9]. Despite this common practice, there is conflicting data about the prevalence of DVT in these infections and the need for CUS [10,11]. In order to better determine this risk, we undertook a systematic review and meta-analysis of the literature to determine the risk of DVT in patients with cellulitis or erysipelas.

Methods

Study Selection

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement for conducting and reporting systematic reviews was used for our meta-analysis [12]. We searched for studies that reported the prevalence of DVT in groups of patients with cellulitis or erysipelas. OVID was used to search Medline using the subject headings "cellulitis", "erysipelas", "soft tissue infections", "venous thrombosis", "thrombophlebitis", and "lower extremity" from 1946 to present. The last search was done on December 1, 2012. References were limited to English language and humans. The Cochrane database was similarly searched. Each author independently screened all retrieved titles and abstracts for full text review. Selection for ultimate inclusion was based on full text review. Disagreement was resolved by mutual consensus.

Abbreviations: DVT, deep vein thrombosis; CUS, compression ultrasound; CI, confidence interval; SSTI, skin and soft tissue infection.

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All references that involved adult patients with cellulitis or erysipelas and reported rates of DVT were included in the review. We excluded pediatric series, case reports, and studies involving other skin and soft tissue infections such as abscess. We included observational studies of selected groups of patients with cellulitis or erysipelas referred for assessment of DVT. We included studies from varied clinical settings, including inpatient, emergency room, and outpatient. Cases were included if DVT was confirmed by compression ultrasound or venography. Cases diagnosed by impedance plethysmography were excluded.

Data Extraction and Quality Assessment

Two investigators assessed all studies meeting inclusion criteria. A standardized data extraction form was used to document patient characteristics such as age, type of soft tissue infection, clinical setting, type of diagnostic test for DVT and the specific definition of DVT used. Study quality assessment was based on the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies [13], except that comparability was not relevant given the design of the included studies.

Data Synthesis and Analysis

The event rate of DVT in patients was estimated and the corresponding 95% confidence interval (CI) from each study was calculated before pooling data. The incidence rates from the included studies were pooled using a random-effects model to calculate an overall DVT rate. Individual and pooled DVT rates with corresponding upper and lower limits were graphed as a forest plot. Between-study heterogeneity was estimated using the I^2 statistic. Subgroup analysis was performed based on type of soft tissue infection, clinical setting, definition of DVT (proximal vs. distal), and study type (prospective vs. retrospective). Statistical significance was assumed for P values less than 0.05. All statistical analysis was performed using Comprehensive Meta Analysis software, version 2 (Biostat, Englewood, New Jersey).

Results

The primary literature search yielded 2,857 articles (Fig. 1). After review of the title and abstracts, 2695 articles were excluded, leaving 162 articles for full text review. Of these, 9 met study inclusion criteria. Tables 1 and 2 outline the characteristics and quality assessment of each study. No randomized controlled studies were identified. All studies were observational studies of patients that were reported as having either cellulitis or erysipelas and who had CUS to assess for DVT. Six of the studies were of patients with cellulitis whereas three were of erysipelas. Most restricted enrollment to patients with lower limb infections, although location wasn't reported in four of the studies. Six of the studies were prospective, with the type of soft tissue infection identified at the time of the ultrasound study, whereas three of the studies were retrospective, with the type of soft tissue infection being defined by record linkage. Other important study variables are shown in Table 1, including whether the study enrolled consecutive patients with cellulitis or erysipelas or whether patients were selected by referral, as well as clinical setting and the definition of DVT used. Of note, five of the studies used whole- leg compression ultrasound and included distal thromboses although only two of these five then reported whether found DVTs were in fact proximal or distal. As noted in Table 2, study quality was primarily limited by patient selection factors. In all of the retrospective studies and four of the prospective studies, reported patients were of select groups referred for ultrasound rather than of consecutive groups with cellulitis/erysipelas. Additionally, in the retrospective studies the presence or absence of DVT on CUS may have affected the enrollment of the patient in the cohort because the coded chart diagnosis may have been after the result of the CUS.

Fig. 2 reports the pooled and individual DVT incidence rates as determined by random-effects meta-analysis, grouped by study type. The total number of patients with either type of infection was 1054, and the total number of DVTs was 18. Eight of the DVTs were proximal, six were distal and 4 were unspecified. Individual study rates ranged from 12.5% (95% CI, 3.1%-38.6%) to 0.5% (95% CI, 0.1% to 1.8%). In general, the three retrospective studies, which contributed 87% of the patients but only half of the DVTs found low rates of DVT. The pooled rate for studies only reporting proximal DVT was 2.1% (95% CI, 0.5%-9.1%). The overall pooled DVT rate including distal DVT was 3.1% (95% CI, 1.9%-4.9%). We found evidence of significant statistical heterogeneity ($I^2 = 64.5\%$; $P = 0.0004$). We explored the heterogeneity by grouping analysis by study type (prospective vs. retrospective), and by clinical variables (proximal vs. whole leg CUS, SSTI type, and clinical setting). Despite the small number of studies in each of these groupings, none resolved the statistical heterogeneity except grouping by study type. When the three retrospective studies are analyzed separately, the pooled incidence rate for DVT is 1.1%

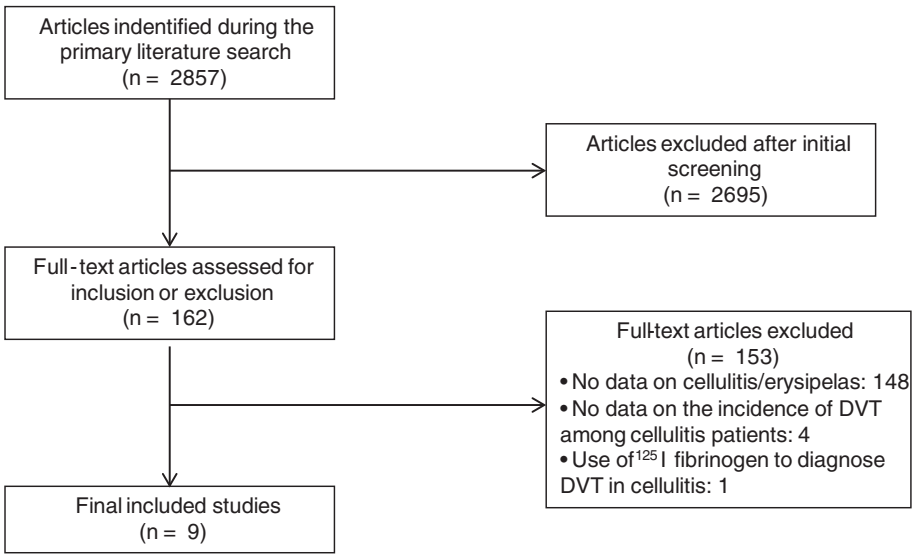

Fig. 1. Flow diagram of study selection process.