Thromboprophylaxis in orthopaedic surgery
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Incidence of deep venous thrombosis after shoulder arthroplasty
Systematic review of literature

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Submitted
ABSTRACT

Introduction
There is a paucity of data regarding the risk of deep vein thrombosis after shoulder arthroplasty. The purpose of this article is to review the available evidence regarding incidence of and risk factors for symptomatic venous thromboembolism (VTE) following shoulder arthroplasty. Mortality after shoulder arthroplasty was also assessed. We hypothesized that the incidence of VTE after shoulder arthroplasty might be higher than the previously reported incidence of VTE after shoulder arthroscopy (VTE: 0.038%, deep venous thrombosis (DVT) 0.029%, pulmonary embolism (PE) 0.017%) and lower than the incidence of VTE after major orthopedic surgery.

Materials and methods
All papers describing symptomatic VTE after shoulder arthroplasty published in English literature retrieved from PubMed were reviewed. Case reports, primary upper limb thrombosis and other non-shoulder surgery-related causes were excluded. A total of five papers were available for analysis: all were large retrospective case series.

Results
The incidence of VTE was 0.59% in 47,998 shoulder arthroplasties. 0.33% of 22,461 procedures which were performed for non-traumatic indications (mostly osteoarthritis and cuff tear arthropathy) and 0.95% from 7,759 procedures for fractures of the proximal humerus. The 90-day incidence of PE (0.28%) was comparable to the 90-day incidence of DVT (0.32%). The mortality rate after shoulder arthroplasty was 0.49%; 0.43% for elective procedures and 3.0% in traumatic indications. The most common risk factors for VTE were comorbidities, traumatic indication for arthroplasty and advanced age.

Conclusions
This review shows that the incidence of VTE and the mortality rate following shoulder arthroplasty is relatively modest but not insignificant. The 90-day incidence of PE was comparable to the 90-day incidence of DVT. Mortality rate was nine times higher for traumatic indications than after elective arthroplasty. The risk of VTE after shoulder arthroplasty is higher than the previously reported risk of VTE after shoulder arthroscopy. Significant risk factors for VTE were the presence of comorbidities and a traumatic indication for shoulder arthroplasty.
INTRODUCTION

Early literature showed that without prophylaxis, the risk of venographically detected deep vein thrombosis (DVT) ranges from 40% to 70% following major orthopedic procedures, such as total hip and knee arthroplasty [1]. Therefore, following lower extremity joint replacement, it became standard practice to use pharmacological thromboprophylaxis[2-4]. Literature from 1980 onwards shows lower venous thromboembolism (VTE) rates, probably because of early mobilization protocols and a significant reduction in the length of hospital stay and maybe because of pharmacological thromboprophylaxis with higher efficacy. The estimated 35-day symptomatic VTE rate without thromboprophylaxis after major orthopedic surgery is currently 4.3% (2.8% DVT and 1.5% pulmonary embolism (PE))[2]. When using thromboprophylaxis by means of LMWH, VTE rate is estimated to be 1.8% (1.25% DVT and 0.55% PE) [2].

Shoulder arthroplasty is considered to cause less immobilization than lower extremity joint arthroplasty, but the procedure is more extensive than uncomplicated shoulder arthroscopy. There is a possibility that the incidence of thromboembolic events may actually be increased following shoulder arthroplasty vs. routine arthroscopy, which is supported by retrospective case series [5-9]. One study suggested that the rate of asymptomatic VTE may be as high as observed following total hip replacement[10].

The aim of the present review is to evaluate the available evidence regarding incidence of and risk factors for symptomatic venous thromboembolism (VTE) following shoulder arthroplasty. Mortality after shoulder arthroplasty was also assessed. We hypothesized that the incidence of VTE after shoulder arthroplasty is higher than the baseline VTE risk of medical patients; higher than the previously reported incidence of VTE after shoulder arthroscopy and lower than the incidence of VTE after major orthopedic surgery.

MATERIAL AND METHODS

A systemic search strategy was used to identify all papers describing symptomatic venous thrombo-embolism (deep venous thrombosis and pulmonary embolism) in shoulder arthroplasty published in English before august 8th 2013. We used the PRISMA statement for systematic reviews [11]. We performed an electronic PubMed, Cochrane and EMBASE database search. The terms (venous) thrombosis, thromboembolism, pulmonary embolism, shoulder surgery and shoulder arthroplasty were used. From the retrieved articles, the reference lists were screened for any relevant papers. Full text copies of these articles were obtained and assessed for eligibility. Case reports, shoulder arthroscopy, primary upper limb thrombosis and other non-shoulder surgery-related causes were excluded.
All papers selected were analyzed for incidence of DVT and pulmonary embolism, risk factors and mortality.

RESULTS

We reviewed 149 papers describing VTE after shoulder arthroplasty (Figure 1). There were no randomized controlled trials or non-randomized comparative studies. Two prospective studies were found [10-12], which actively screened for asymptomatic DVT. In both studies, thromboprophylaxis was giving by means of pneumatic compression devices intra-operatively and aspirin post-operatively. These studies were not included in the analysis, as we defined symptomatic VTE as the primary outcome measure. Three review articles were identified [13-15], from which the relevant studies were already included in our analysis and two papers described guidelines [16,17]; all five were excluded.

Seven level II retrospective database analyses (describing prospectively collected data) were found, of which 3 studies described the same patient population[6,18,19]. Ultimately, 5 studies[5-9] were eligible for this review (Table 1). Four studies described the 90-day VTE rate, and one study[9] described VTE rate during surgical admission only (4.7 days).

Incidence of VTE

The overall incidence of symptomatic VTE after shoulder arthroplasty was 0.59% in 47,998 procedures and ranged from 0.24 to 6.8% (Table 1). The 90-day incidence of PE (0.28%) was comparable to the 90-day incidence of DVT (0.32%). All but one study reported the incidence of VTE to be higher after hemi arthroplasty than after elective total shoulder arthroplasty. The VTE rate was higher in shoulder arthroplasty for traumatic indications (0.95%) than after elective arthroplasty (0.33%). Mortality rate was also higher for traumatic indications (3.0%) than after elective arthroplasty (0.43%) (Table 2).

Risk factors

Risk factors for VTE in the studied articles are shown in Table 3. Most common statistically significant risk factors were the presence of comorbidities and a traumatic indication for shoulder arthroplasty.

Diagnosis of VTE

In all 5 studies, the method of detection of DVT and PE was not documented. Diagnostic codes (ICD-9-CM and ICD-10) were used to extract diagnoses of DVT and PE from the
Table 1. Symptomatic venous thromboembolic complications of shoulder arthroplasty

<table>
<thead>
<tr>
<th>Author</th>
<th>Procedures (n)</th>
<th>VTE</th>
<th>DVT</th>
<th>PE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n,%)(n,%)(n,%)</td>
<td>Total</td>
<td>Total</td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TSP</td>
<td>HA</td>
<td>TSP</td>
</tr>
<tr>
<td>Navarro</td>
<td>2574</td>
<td>1388</td>
<td>1186</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(54)</td>
<td>(46)</td>
<td>(1.01)</td>
</tr>
<tr>
<td>Singh</td>
<td>4019</td>
<td>2588</td>
<td>1431</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>(3480 patients)</td>
<td>(64)</td>
<td>(36)</td>
<td>(1.2)</td>
</tr>
<tr>
<td>Fangh</td>
<td>15288</td>
<td>5044</td>
<td>10244</td>
<td>91</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(33)</td>
<td>(67)</td>
<td>(0.6)</td>
</tr>
<tr>
<td>Jameson</td>
<td>12358</td>
<td>4061</td>
<td>8297</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(33)</td>
<td>(67)</td>
<td>(0.24)</td>
</tr>
<tr>
<td>Lyman</td>
<td>13759</td>
<td>4931</td>
<td>8828</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(36)</td>
<td>(64)</td>
<td>(6.8)</td>
</tr>
<tr>
<td>Total (n,%)</td>
<td>47998</td>
<td>18012</td>
<td>29986</td>
<td>283</td>
</tr>
</tbody>
</table>

VTE = venous thromboembolism
DVT = deep venous thrombosis
PE = pulmonary embolism
TSP = total shoulder arthroplasty
HA = hemi arthroplasty
NHS = National Health Service
<table>
<thead>
<tr>
<th>Author</th>
<th>Elective procedure</th>
<th>Trauma procedure</th>
<th>Elective procedure</th>
<th>Trauma procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence of VTE</td>
<td>Mortality</td>
<td>Incidence of VTE</td>
<td>Mortality</td>
</tr>
<tr>
<td></td>
<td>Total (n,%)</td>
<td>Total (n,%)</td>
<td>Total (n,%)</td>
<td>Total (n,%)</td>
</tr>
<tr>
<td>Navarro</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16/1988</td>
<td>10/586 (1.71)</td>
<td>4/1988 (0.20)</td>
<td>1/646 (0.15)</td>
<td>9/586 (1.54)</td>
</tr>
<tr>
<td></td>
<td>15/1342 (1.12)</td>
<td>3/1342 (0.22)</td>
<td>1/646 (0.15)</td>
<td>8/540 (1.48)</td>
</tr>
<tr>
<td>Fangh</td>
<td>50/5044 (0.99)*</td>
<td>54/10244 (0.53)</td>
<td></td>
<td>145/5044 (2.87)*</td>
</tr>
<tr>
<td>41/10244</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jameson</td>
<td>14/2129 (0.66)</td>
<td>38/10229 (0.37)</td>
<td>14/2129 (0.66)</td>
<td>80/2129 (3.76)</td>
</tr>
<tr>
<td>16/10229</td>
<td>8/4061 (0.20)</td>
<td>9/4061 (0.22)</td>
<td>8/6168 (0.13)</td>
<td>80/2129 (3.76)</td>
</tr>
<tr>
<td>Total (n,%)</td>
<td>74/7759 (0.95)</td>
<td>96/22461 (0.43)</td>
<td>234/7759 (3.0)</td>
<td></td>
</tr>
</tbody>
</table>

VTE = venous thromboembolism
TSP = total shoulder arthroplasty
HA = hemi arthroplasty
* significant difference (P <0.05)
Figure 1. Algorithm showing search methods, according to PRISMA methodology

Table 3. Risk factors for VTE

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Female gender</th>
<th>Obesity BMI 25.5-29.9</th>
<th>History of DVT/PE</th>
<th>Comorbidity (Charlson Index)</th>
<th>Indication (trauma vs. elective)</th>
<th>Procedure type (hemi vs. TSP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Navarro</td>
<td>-</td>
<td>-</td>
<td>Excluded</td>
<td>-</td>
<td>-</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Singh</td>
<td>&gt;70 *</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>≥ 1 *</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Fangh</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>&gt; 1 *</td>
<td>-</td>
<td>*</td>
<td>-</td>
</tr>
<tr>
<td>Jameson</td>
<td>NS</td>
<td>-</td>
<td>Excluded</td>
<td>1 *</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lyman</td>
<td>10-year increase in age *</td>
<td>NS</td>
<td>-</td>
<td>-</td>
<td>NS</td>
<td>*</td>
<td>NS</td>
</tr>
</tbody>
</table>

* significant difference (P <0.05); NS = no significant difference

BMI = Body Mass Index
DVT = deep venous thrombosis
PE = pulmonary embolism
TSP = total shoulder prosthesis
databases. When a DVT was present, the location of the thrombus was reported by only one study [5]: 7 upper limb (1 contra-lateral) and 6 lower limb DVTs were described.

**Prophylaxis**
Three studies did not mention if thromboprophylaxis was used. Singh et al. [6] noted that thromboprophylaxis was not routinely used. Jameson and colleagues [8] reported that the majority of patients should get thromboprophylaxis according to the NHS guidelines.

**DISCUSSION**

**Main findings**
The overall 3-month incidence of symptomatic VTE after shoulder arthroplasty was 0.59% in 47,998 procedures and ranged from 0.24 to 6.8%. The 90-day incidence of PE (0.28%) was comparable to the 90-day incidence of DVT (0.32%). All but one study reported the incidence of VTE to be higher after hemi arthroplasty than after total shoulder arthroplasty. The VTE rate was higher in shoulder arthroplasty for traumatic indications (0.95%) than after elective arthroplasty (0.33%). The mortality rate was higher for traumatic indications (3.0%) than after elective arthroplasty (0.43%).
The most common significant risk factors were the presence of comorbidities (such as cardiac, pulmonary, renal, diabetes, etc,) and a traumatic indication for shoulder arthroplasty.
The data were retrieved from five level II retrospective database analyses. Data were comparable, as their study design for the main outcomes (VTE, type of prosthesis) were almost identical. One study [6] did not describe the difference in type of prosthesis (hemi vs. total arthroplasty). Data on indication for surgery (traumatic vs. elective) and mortality could only be retrieved from three of the five studies.

An interesting finding is, that the incidence of PE (0.28%) was comparable to the incidence of DVT (0.32%). Lyman et al. [9] described higher DVT rates, probably because they described VTE rate during admission only (4.7 days on average). After total hip and total knee replacement, reported DVT rate is always much higher than PE rate. The main difference between upper extremity and lower extremity surgery may be explained by adequate early mobilization, causing less DVTs after shoulder surgery. The question remains why the incidence of PE is relatively high after shoulder arthroplasty. Would intramedullary reaming of the upper extremity lead to more PEs? The overall PE rate after shoulder surgery without thromboprophylaxis is lower than the PE rate after lower extremity arthroplasty [2]. The location of the thrombus might be a risk factor for de-
Incidence of deep venous thrombosis after shoulder arthroplasty will probably be underestimated, as this review included only symptomatic VTE. The incidence of asymptomatic DVT, as detected by ultrasound, is described to be as high as 13% in 100 patients, up to 12 weeks after surgery [10]. There is a relation between asymptomatic DVT and symptomatic VTE [24,25]. It remains unclear which percentage of asymptomatic lower leg thrombi propagate proximally from where they might cause pulmonary embolism. In symptomatic calf vein clots, 20% propagate proximally [26] and asymptomatic proximal DVTs have demonstrated a risk of symptomatic PE in 40% [27]. Both phenomena (VTE/DVT) are symptoms of the same disease process of hypercoagulability, a condition we believe should be prevented.

Compared to shoulder arthroscopy, VTE rates after shoulder arthroplasty are higher. In their systematic review, Datani et al. described an overall VTE rate of 0.038% in 92440 patients, a PE rate of 0.017% and a DVT rate of 0.029% after shoulder arthroscopy. This risk is similar to the VTE risk in the general population [28].

The higher VTE rate after shoulder arthroplasty could be explained by several factors. First, the mean age of patients undergoing arthroplasty is higher. Increased age is a known risk factor for VTE [2]. The duration of the operation is substantially longer in arthroplasty. Operations lasting more than 60 minutes are also described as an independent risk factor for VTE [2]. Arthroplasty is performed in beach chair position, while in shoulder arthroscopy both beach chair and lateral decubitus positions can be chosen. Beach chair position may lead to more VTE’s, due to venous stasis in the legs [29]. Contrary to this statement, in their review Datani et al. found more upper extremity DVTs during lateral decubitus position (14 cases) than in beach chair position (4 cases) during arthroscopy of the shoulder, based on small numbers [13,30]. The incidence of upper extremity DVT may be attributed to traction and subsequently reduced limb perfusion [31]. Intramedullary reaming during arthroplasty placement may lead to (fatty) embolus formation [32]. Finally, intimal damage to the axillary vein during arthroplasty through (in)direct trauma may be caused by traction, repeated rotation of the humerus or direct pressure of retractors [10,33,34].
Limitations
General limitations for retrospective database analysis of prospectively collected data apply: The diagnosis of VTE was extracted from ICD codes. Coding errors could occur. The exact method of detection of VTE (Doppler/CT angiogram/ventilation perfusion scan) is not described. There are no data on the location of the thrombus (upper or lower extremity).
Data concern admitted or re-admitted patients within 90 days after shoulder arthroplasty: there are no data on the outpatients diagnosed with and treated for DVT. (One study only included patients with VTE during surgical admission) [9]. There are no data on the use or type of VTE prophylaxis. No data on cause of death are available. Patients who died at home are not accounted for.
However, when a rare complication, such as VTE is investigated, large database studies are needed, because prospective, single centre studies would have to include thousands of patients and would take many years to perform. While randomized controlled trials are not available (for this same reason), the interpretation of database analyses is justified.
Recommendations regarding the use of thromboprophylaxis following shoulder arthroplasty cannot be made based on this review. A randomized controlled trial should be performed, including sufficient patients to detect a difference between the incidence of VTE with (0.25%) and without thromboprophylaxis (0.59%).

CONCLUSION

The purpose of our study was to review the available evidence regarding incidence of and risk factors for symptomatic venous thromboembolism (VTE) following shoulder arthroplasty. Mortality was also investigated. The five retrospective database studies indicate a variable, low incidence of VTE and low mortality after shoulder arthroplasty. Mortality rate was nine times higher for traumatic indications than after elective arthroplasty.
Significant risk factors for VTE were the presence of comorbidities and a traumatic indication for shoulder arthroplasty. Recommendations regarding the use of thromboprophylaxis following shoulder arthroplasty cannot be made based on this review.
REFERENCES


