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Venous thromboembolism following surgical management of proximal humerus fractures: a systematic review

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Background: Currently, there is limited information on the incidence of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) after surgical treatment of proximal humerus fractures (PHFs). Therefore, the purpose of this systematic review is to evaluate the incidence of VTE, DVT, and PE following surgery for PHFs.

Methods: A comprehensive search of several databases was performed from inception to May 27, 2022. Studies were screened and evaluated by 2 reviewers independently utilizing the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. Only original, English studies that evaluated the incidences of VTE following surgical management of PHFs were included. Surgical procedures consisted of shoulder arthroplasty (SA) including both hemiarthroplasty (Hemi) and reverse shoulder arthroplasty (RSA) in addition to open reduction and internal fixation (ORIF). A pooled incidence for postoperative DVT, PE, and overall VTE was reported.

Results: Twelve studies met the inclusion and exclusion criteria, encompassing a total of 18,238 patients. The overall DVT, PE, and VTE rates were 0.14%, 0.59%, and 0.7%, respectively. VTE was more frequently reported after SA than ORIF, (1.27% vs. 0.53%, respectively). Among SA patients, a higher rate of DVT was seen with RSA (1.2%) with the lowest DVT rate was observed for ORIF with 0.03%.

Conclusions: Symptomatic VTEs following surgical treatment of PHFs, are rare, yet still relevant as a worrisome postoperative complication. Among the various procedures, VTE was the most frequently reported after SA when compared to ORIF, with RSA having the highest VTE rate.

Venous thromboembolism (VTE) is not an uncommon complication following orthopedic surgery, with reported rates as high as 10.7%.[14,26,27,31] Importantly, VTE has been recognized as a major contributor to morbidity and mortality.[25,28] For example, a study evaluating total hip arthroplasty and total knee arthroplasty patients found an inhospital mortality rate of 7.1% in those with VTEs compared to 0.3% for those without.[28] The mean total costs of inpatient care have also been shown to be nearly twice as high in those with VTE compared to those without VTE following major orthopedic surgery.[20] The importance of these numbers has driven increased interest in also understanding VTE following shoulder surgery.

In the field of shoulder arthroplasty (SA), a recent systematic review by Na et al[18] including a total of 9 studies with 12,566 shoulders found an overall incidence rate of 0.81% for VTE, with an associated mortality rate of 4.1%. Hypoalbuminemia (<3.5 g/dL), a prolonged length of stay, and African American ethnicity were found to be independent risk factors for VTE within 30 days following primary total shoulder arthroplasty (TSA) in a large database study.[15] Similarly, a higher body mass index, older age, and longer operative duration have also been shown to be independent risk factors for 30-day postoperative VTE.[34] In the field of shoulder arthroscopy, Triplet et al[30] conducted a systematic review of 13 studies with 32,407 patients undergoing shoulder arthroscopy and found an overall VTE rate of 0.21%, with those specifically

This study was exempt by the Mayo Clinic Institutional Review Board.

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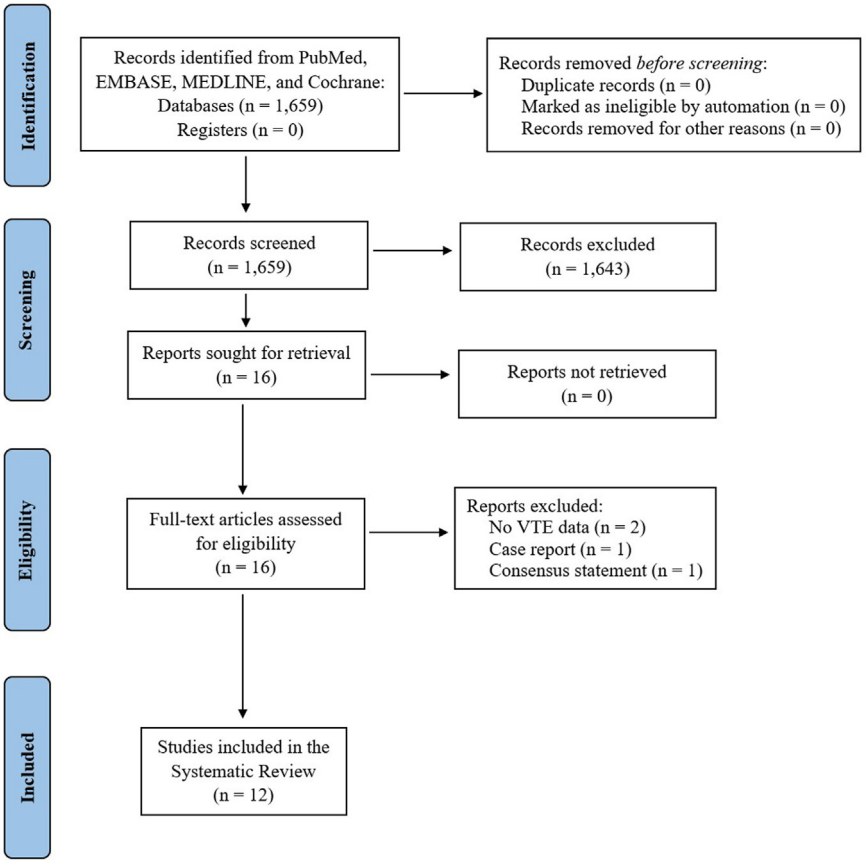

Figure 1 Study inclusion according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. *VTE,* venous thromboembolism.

undergoing arthroscopic rotator cuff repair (RCR) found to have a higher rate of 1.04% for VTE. Risk factors for VTE within 30 days of arthroscopic RCR have been shown to include a surgery longer than 80 minutes, use of general anesthesia, and an American Society of Anesthesiologists (ASA) class of 3 or 4.[24] A high altitude (>4000 feet) operative setting has also been shown to increase the risk for VTE within 90 days following arthroscopic RCR.[2]

Trauma patients have an even higher risk for VTE due to pathophysiological changes in coagulation pathways and the systemic inflammatory response from tissue injury[16,17,23]. This may create unique and complex challenges in VTE prophylaxis for patients with proximal humerus fractures (PHFs). However, there are limited guidelines on perioperative VTE prevention and management after shoulder surgery in the trauma setting.[5] A better understanding of the incidence of VTE in this patient population will allow us to establish more effective perioperative guidelines for decreasing morbidity, mortality, and costs. Therefore, the purpose of this study was to systematically establish the incidence of VTE (including deep vein thrombosis [DVT] and pulmonary embolism [PE]) following surgical management of PHFs.

Materials and methods

This study was conducted in concordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA) guidelines (Fig. 1).

Eligibility criteria

Standardized inclusion and exclusion criteria were used to determine study eligibility. The inclusion criteria were as follows: (1) involved surgical management of PHFs and (2) reported incidence of DVT, PE, and overall VTE. The exclusion criteria were as follows: (1) not published in English language, (2) no original, extractable clinical data (i.e., review articles, commentaries, and letters to the editor), and (3) no full-text available. Patients undergoing any form of surgery for a PHF were included, including open reduction and internal fixation (ORIF) and SA using either hemiarthroplasty (Hemi) or reverse shoulder arthroplasty (RSA).

Search strategy

The literature search was designed and conducted by an experienced biomedical librarian (L.C.H.). A systematic literature search was performed on June 1, 2022, using several databases for all articles available on the databases from inception to June 1, 2022. The databases included Ovid MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, Ovid Embase, Ovid Cochrane Central, Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, Web of Science, and Scopus. Controlled vocabulary supplemented with keywords was used to search for studies describing VTE after surgery for PHFs. The detailed strategy listing all search terms used and how they are combined is available in the Supplementary Appendix S1.

Data collection and analysis

Studies were screened by 2 reviewers (J.W.S and R.M.) independently by title and/or abstract using the inclusion and exclusion criteria. All potentially eligible studies identified by title and abstract screening were then evaluated by reading the full-text to determine the final inclusion. Any discrepancies were resolved by

Table I
Study characteristics and patient demographics.

Study	LOE	No. of patients	Mean age y ± SD, (range)	Mean FU (mo)	Shoulder arthroplasty	Hemi	RSA	TSA	ORIF
Andres-Cano et al[1]	IV	21	72 ± 6.8	26.3 ± 10.9	21	19	0	0	0
Chand et al[3]	IV	21	NR	3*	21	0	21	0	0
Dillon et al[6]	III	1045	72 ± 12	40.9 ± 27.9	1045	961	72	12	0
Heyer et al[8]	IV	92	58.1	6	12	4	8	0	80
Hoxie et al[9]	IV	137	63.1	NR	37	37	0	0	102
Imberti et al[10]	III	28	55.65	3*	0	0	0	0	28
Jameson et al[11]	II	4696	65	3*	2129	2129	0	0	2567
Kissin et al[12]	IV	17	70	3*	17	11	5	1	0
Kolz et al[13]	IV	151	NR	50.64	151	64	85	2	0
Navarro et al[19]	III	586	NR	3*	586	540	23	23	0
Widmer et al[32]	II	50	68.8	12	10	10	0	0	40
Petrigliano et al[22]	IV	11,394	61.6 ± 20.5	3*	0	0	0	0	11,394
Summary Statistics		**Total 18,238**	**Range 55.7-72.0**	**Range 3-40.9**	**Total 4029**	**Total 3775**	**Total 214**	**Total 38**	**Total 14,211**

LOE, level of evidence; *SD*, standard deviation; *FU*, follow-up; *Hemi*, hemiarthroplasty; *RSA*, reverse shoulder arthroplasty; *TSA*, total shoulder arthroplasty; *ORIF*, open reduction internal fixation; *NR*, not reported.
*These studies reported on 90-day complication rate.

Table II
Surgical treatment of proximal humerus fracture venous thromboembolism results.

Study	Patients, n	DVT, n	PE, n	VTE, n
Andres-Cano et al[1]	21	0	0	0
Chand et al[3]	21	0	0	0
Dillon et al[6]	1045	8	10	18
Heyer et al[8]	92	0	3	3
Hoxie et al[9]	137	0	7	7
Imberti et al[10]	28	0	0	0
Jameson et al[11]	4696	9	19	24
Kissin et al[12]	17	0	0	0
Kolz et al[13]	151	3	3	5
Navarro et al[19]	586	5	6	10
Widmer et al[32]	50	0	0	0
Petrigliano et al[22]	11,394	0	60	60
Total	18,238	25	108	127
Incidence	-	0.14%	0.59%	0.70%

DVT, deep vein thrombosis; *PE*, pulmonary embolism; *VTE*, venous thromboembolism.

Table III
Deep vein thrombosis, pulmonary embolism, and venous thromboembolism rates reported for each surgical procedure.

Surgical procedure	DVT, % (n)	PE, % (n)	VTE, % (n)
ORIF	0.03 (4)	0.52 (74)	0.53 (76)
SA	0.52 (21)	0.84 (34)	1.27 (51)
Hemi	0.48 (18)	0.9 (34)	1.27 (48)
RSA	1.4 (3)	0	1.4 (3)

DVT, deep vein thrombosis; *PE*, pulmonary embolism; *VTE*, venous thromboembolism; *SA*, shoulder arthroplasty; *Hemi*, hemiarthroplasty; *RSA*, reverse shoulder arthroplasty; *ORIF*, open reduction internal fixation.

consensus. The incidence of DVT, PE, and overall VTE was extracted from each study. After data extraction, a pooled incidence for postoperative DVT, PE, and overall VTE was reported.

Study methodology assessment

Study methodology was assessed by 2 reviewers independently using the Methodological items for non-randomized studies (MINORS).[29] The MINORS score was categorized for each study as follows: 0 < MINORS score < 6 to indicate a very low quality of evidence, 6 ≤ MINORS score < 10 to indicate low quality of evidence, 10 ≤ MINORS score < 14 to indicate fair quality of evidence, and MINORS score ≥ 14 to indicate good quality of evidence.[7]

Statistical analysis

Due to the heterogeneity in data reporting among the included studies, no statistical analysis was able to be performed. Rather, this systematic review focused on reporting overall incidence of DVT, PE, and overall VTE following all surgeries for PHFs.

Results

Twelve studies met the inclusion and exclusion criteria and were analyzed in this review.[1,3,6,8-13,19,22,32] Two were level II evidence,[11,32] 3 were level III evidence,[6,10,19] and 7 were level IV evidence.[1,3,8,9,12,13,22] The total pooled number of shoulders with surgically treated PHFs was 18,240 in 18,238 patients. This cohort had a mean age range of 55.7-72 years. ORIF was the most common procedure (n = 14,211, 77.9%), followed by Hemi (n = 3,775, 20.7%), RSA (n = 214, 1.2%), and TSA (n = 38, 0.21%). Table I shows the patient demographics and study characteristics.

The overall DVT, PE and VTE rates were 0.14%, 0.59%, and 0.70%, respectively (Table II). DVT and PE were more frequently reported for SA, with a VTE incidence rate of 1.27% compared to 0.53% for ORIF (Table III). Among SA patients, a higher rate of DVT was observed in RSA (1.2%) relative to Hemi (0.48%). The lowest DVT rate was observed for ORIF with 0.03%.

The MINORS score was calculated for each study and the results are summarized in Table IV. The mean MINORS score was 13.4 ± 0.7 indicating moderate methodological bias of the studies in the review. After categorizing each study methodology, 6 were considered of good quality, and 6 were considered of fair quality.

Discussion

This systematic review aimed to find the incidence of VTE in surgically treated patients with a PHF. The overall DVT, PE, and VTE rates were 0.14%, 0.59%, and 0.7%, respectively. Among the various surgical treatments for PHFs, the pooled VTE rate was 1.27% in SA and 0.53% in ORIF, respectively. This difference may be explained by differences within age and comorbidities between groups. Clinically, SA is more frequently indicated for older patients with comorbidities and ORIF for healthier and younger patients. Concordantly, our review displayed lower mean ages in ORIF compared to those in SA.

The PE incidence rate was also slightly higher for SA (0.84%) than for ORIF (0.52%). Very low rates of DVT were reported for ORIF (0.03%) with a much higher rate seen for SA (0.52%). Within

Table IV
Methodological items for non-randomized studies score.

Study	MINORS score	Interpretation
Andres-Cano et al[1]	12	Fair
Chand et al[3]	13	Fair
Dillon et al[6]	14	Good
Heyer et al[8]	13	Fair
Hoxie et al[9]	13	Fair
Imberti et al[10]	14	Good
Jameson et al[11]	14	Good
Kissin et al[12]	13	Fair
Kolz et al[13]	14	Good
Navarro et al[19]	14	Good
Widmer et al[32]	13	Fair
Petrigliano et al[22]	14	Good
Total, mean ± SD (range)	13.4 ± 0.67 (12-14)	

MINORS, methodological items for non-randomized studies; *SD*, standard deviation. All included studies are observational noncomparative studies with an ideal score of 16.

arthroplasty patients, a higher DVT rate was observed for RSA (1.4%) than for Hemi (0.48%). Previous studies[10,18] have found that a longer operative time and advanced age are VTE risk factors in patients undergoing shoulder arthroplasty, which may explain higher rates of DVT in RSA compared to Hemi.

General VTE risk factors include obesity, advanced age, diabetes, trauma, immobilization, cancer, and hypertension, among others.[4,18] Three studies in this review identified specific risk factors for VTE with age being the most commonly reported.[10,13,22] Petrigliano et al[22] in a large series of over 9000 patients treated with ORIF described an increased risk of PE associated with male sex (odds ratio (OR) = 2.2, $P = .007$) and patient age ≥ 75 years (OR = 3.6, $P = .001$). In another study comprising patients treated with arthroplasty aged ≥ 70 years was found to have an OR of 3.54 (95% confidence interval, 1.28-9.81 [$P = .00\ 7$]) for VTE.[13]

VTE prophylaxis was described in 7 studies with mechanoprophylaxis and early ambulation being the most reported measures.[1,8-11,13,32] Two studies[1,11] reported the use of low molecular weight heparin with no association found between the general use of chemoprophylaxis and VTE prevention. Jameson et al[11] performed a large database study in which 59% of patients in ORIF group and 88% of patients in Hemi group received low molecular weight heparin and concluded that chemoprophylaxis may not be required even for high-risk patients. Though described adverse events (including major and minor bleeding) associated with the use of chemoprophylaxis are rare,[21,33] its universal use in surgically treated patients with PHF may be unnecessary. Selected cases such as patients with clotting disorders, ≥75 years, pathologic fractures, body mass index > 30, active smokers, patients diagnosed with cancer, or who sustain poly trauma may benefit from additional antithrombotic measures.[23-25]

There are several limitations to account for in this systematic review. First, most studies displayed a lower evidence level with no randomized controlled or prospective comparative studies included. Observational and registry-based studies included have an inherent bias that must be considered. The low incidence of VTE found in our study highlights the fact that our observations may be underpowered and may not represent the real rate of VTE in the entire population. Moreover, the lower numbers of RSAs and TSAs have to be considered when interpreting results. In the future, larger, prospective, multicenter studies would be helpful to better capture the real prevalence of VTE in the population of patients being surgically treated for PHFs.

Conclusion

Symptomatic VTEs following surgical treatment of PHFs, are rare, yet still relevant as a postoperative complication. Among the various procedures, VTE was the most frequently reported after SA when compared to ORIF, with RSA having the highest VTE rate. While current literature does not support the use of chemoprophylaxis in all cases, patients with elevated risk profiles treated with SA should be closely monitored for the development of subsequent VTE.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.xrrt.2023.06.003.

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