J Shoulder Elbow Surg (2019) 28, 587–595

ELSEVIER

Journal of Shoulder and Elbow Surgery

www.elsevier.com/locate/ymse

Heterotopic ossification after total elbow arthroplasty: a systematic review

Eva Y. Liu, BHSc[a], Alexandra Hildebrand, BHSc[a], Nolan S. Horner, MD[b], George S. Athwal, MD, FRCSC[c], Moin Khan, MD, MSc, FRCSC[b,*], Bashar Alolabi, MD, MSc, FRCSC[b]

[a]*Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada*
[b]*Department of Surgery, St Joseph's Healthcare, Hamilton, ON, Canada*
[c]*Roth | McFarlane Hand and Upper Limb Centre, London, ON, Canada*

Background: Heterotopic ossification (HO) is a known complication that can arise after total elbow arthroplasty (TEA). In most cases, it is asymptomatic; however, in some patients, it can limit range of motion and lead to poor outcomes. The objective of this review was to assess and report the incidence, risk factors, prophylaxis, and management of HO after TEA.

Methods: A systematic search was conducted using MEDLINE, Embase, and PubMed to retrieve all relevant studies evaluating the occurrence of HO after TEA. The search was performed in duplicate, and a quality assessment of all included studies was performed.

Results: A total of 1907 studies were retrieved, of which 45 were included involving 2256 TEA patients. HO was radiographically present in 10% of patients and was symptomatic in 3%. Fewer than 1% of patients went on to undergo surgical excision of HO, with outcomes after surgery reported as good or excellent as assessed by range of motion and the Mayo Elbow Performance Score. HO appears more likely to develop in patients undergoing TEA because of ankylosis, primary osteoarthritis, and distal humeral fractures. Surgical intervention is more likely to be required in patients in whom HO develops after TEA performed for ankylosis and post-traumatic osteoarthritis.

Conclusion: HO is an uncommon complication after TEA, with most patients in whom HO develops being asymptomatic and requiring no surgical management. Routine HO prophylaxis for TEA is not supported by the literature. The effectiveness of prophylaxis in high-risk patients is uncertain, and future studies are required to clarify its usefulness.

Level of evidence: Level IV; Systematic Review

Keywords: Total elbow arthroplasty; heterotopic ossification; complication; elbow arthritis; elbow trauma; fracture

Total elbow arthroplasty (TEA) is a well-accepted surgical procedure for rheumatoid arthritis, acute fracture in elderly patients, osteoarthritis, and other pathologic conditions of the elbow.[55] Previous studies have shown that TEA can considerably improve elbow function and allow patients to complete

*Reprint requests: Moin Khan, MD, MSc, FRCSC, St Joseph's Healthcare Hamilton, 50 Charlton Ave E, Hamilton, ON L8N 4A6, Canada.
E-mail address: khanmm2@mcmaster.ca (M. Khan).

1058-2746/$ - see front matter © 2018 Journal of Shoulder and Elbow Surgery Board of Trustees. All rights reserved.
https://doi.org/10.1016/j.jse.2018.10.003

important daily activities, such as eating and dressing.[32,44] However, TEA is still a relatively uncommon procedure with a higher rate of complications and revision procedures compared with hip or knee arthroplasty.[44,55] One such complication is heterotopic ossification (HO).

HO refers to the formation of bone in extraskeletal soft tissue, which can occur after musculoskeletal or nervous system trauma. The musculoskeletal trauma can arise owing to fractures, joint dislocations, burns, or surgical interventions. During the healing process, mesenchymal cells may inappropriately differentiate into osteogenic precursor cells, resulting in the formation of ectopic bone.[48] HO has been most extensively studied in the total hip arthroplasty (THA) literature and other procedures involving the hip joint.[26,39] In most cases, HO appears as asymptomatic bone formation near the site of surgery and typically has little to no impact on functional outcomes. However, excessive HO formation may decrease joint range of motion (ROM) to a degree requiring surgical excision.[45] Nonsteroidal anti-inflammatory drugs (NSAIDs) and radiotherapy are often used as prophylactic treatment to reduce the risk of HO after surgery; however, the effectiveness in preventing HO after TEA requires further investigation.

Although many studies have investigated HO after major hip surgery, limited evidence exists regarding the reporting of HO after TEA. The objective of this systematic review was to provide a comprehensive review of the literature to present available evidence regarding the incidence, potential risk factors, prophylaxis, and management of HO after TEA.

Methods

This study was conducted according to the methodology described in the *Cochrane Handbook for Systematic Reviews of Interventions* and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Search strategy and eligibility

A search was conducted in Ovid Medline (1946 to week 2 of January 2018), Embase (1974 to week 2 of January 2018), and PubMed (up to January 16, 2018) by 1 reviewer using the keyword "elbow" combined with "arthroplasty" combined with either "complication," "ossification," or "heterotopic ossification" limited to humans (Appendix S1). The inclusion criteria were (1) studies evaluating HO after TEA and complication management, (2) studies published in English, and (3) studies on humans. We excluded (1) nonsurgical studies, (2) studies that involved overlapping patient populations, (3) review articles, and (4) basic science studies. In cases in which duplicate studies contained overlapping patient populations, the study with the larger patient population was included. If a follow-up study of the same patient population was identified, the more recent study was included.

Study selection

Two reviewers (E.Y.L. and A.H.) independently screened the titles and abstracts of the studies identified through the literature search. Relevant articles were retrieved and rescreened for eligibility based on the full-text article. Any disagreements were resolved either by consensus or through discussion with a third reviewer. The references of the included articles were hand searched to identify additional relevant studies.

Data collection

Data were collected independently by 2 reviewers (E.Y.L. and A.H.). Disagreements were resolved either by consensus or through discussion with a third reviewer. Information collected included study characteristics (eg, authors, article title, year of publication, study design, and level of evidence), patient information (eg, age, percentage of male vs female patients, and sample size), surgical technique and prosthesis, outcomes after TEA, complications, and revision procedures owing to complications. In addition, the number of HO patients, grading or classification of HO, symptoms, prophylactic measures to prevent HO, and management were recorded.

Quality assessment of included studies

The quality of the studies was assessed by 2 reviewers (E.Y.L. and A.H.) using the Methodological Index for Non-Randomized Studies (MINORS) appraisal tool for observational studies and the Cochrane risk-of-bias tool for randomized controlled trials. A score of 0, 1, or 2 was assigned to each of the 12 criteria on the MINORS checklist, resulting in a maximum score of 16 for noncomparative studies and 24 for comparative studies. MINORS scores were categorized as follows: 0 to 6 was considered very low quality of evidence; 7-10, low quality of evidence; 10-14, fair quality of evidence; and 15 or greater, good quality of evidence.

Randomized controlled trials were appraised using the Cochrane risk-of-bias tool, and a rating of low risk, high risk, or unclear risk of bias was assigned with respect to potential selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.

Statistical analysis

Descriptive statistics (eg, mean, standard deviation, and range) were calculated and presented where applicable. Weighted means and weighted standard deviations, which take the different sample sizes of the studies into consideration, were also presented when possible. A κ statistic indicating inter-reviewer agreement was calculated for all screening stages. The calculated κ was categorized as follows: 0.81 to 0.99 indicated excellent agreement; 0.61 to 0.80, substantial agreement; 0.41 to 0.60, moderate agreement; 0.21 to 0.40, fair agreement; and 0.20 or less, slight agreement.[30]

Results

Eligibility

The literature search identified a total of 3139 studies, yielding 1907 studies after removal of duplicates. Title and abstract screening refined this to 150 studies, of which 46 were included after full-text review. Three more studies were identified through the references of the included studies, and 4 were

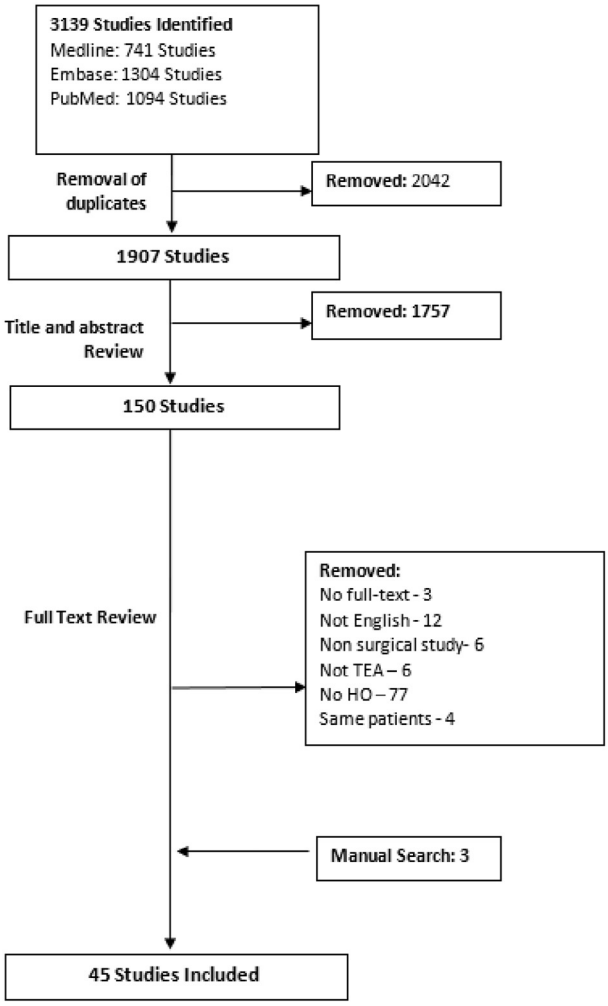

Figure 1 Included studies. *TEA*, total elbow arthroplasty; *HO*, heterotopic ossification.

excluded because of inclusion of the same patient populations (Fig. 1). In total, 45 studies were included in this review. Substantial agreement was found between reviewers at the title and abstract ($\kappa = 0.624$; 95% confidence interval [CI], 0.548-0.701) and full-text ($\kappa = 0.656$; 95% CI, 0.521-0.792) review stage.

Study characteristics

A total of 2256 patients underwent TEA in the included studies. The mean sample size was 50 (SD, 96; range, 1-654). HO developed postoperatively in 233 (10%) of the included patients. On average, HO developed in 5 patients (SD, 9 patients; range, 1-50 patients) per study. In total, 59 patients (3%) were symptomatic and 13 (0.6%) underwent revision because of HO. An HO patient was classified as symptomatic if (1) the study authors reported symptoms, (2) the patient underwent revision because of HO, or (3) the patient had less than 120° of flexion (Appendix S2).[1-9,11-19,21,22,24,25,27-29,31,33-38,40-43,46,47,49-52,54,56,57]

Demographic characteristics

Female patients comprised 73% (SD, 2.3%; range, 19%-100%) of the included patients, and the weighted mean age of the patients was 62 years (SD, 1.4 years; range, 31-85 years). Ten studies (TEA sample comprising 191 patients) reported the sex of the HO patients. A total of 18 HO patients were reported in these studies, and 12 (67%; SD, 22%; range, 0%-100%) of them were female patients. Ten studies (TEA sample comprising 221 patients) reported the mean age of the HO patients. A total of 18 HO patients were included, and the mean age was 55 years (SD, 10.1 years; range, 23-71 years).

Study quality

Of the 45 included studies, 38 (84%) were level IV studies that evaluated outcomes and complications of TEA case series. All but 1 of the included studies (44 studies) were nonrandomized in design, and their quality was assessed using the MINORS score. The 1 randomized controlled trial included was evaluated using the Cochrane risk-of-bias tool (Appendix S3). The mean MINORS score for noncomparative studies was 10 ± 1.9 of 16 (40 studies), indicating that the noncomparative studies were poor in quality. The mean MINORS score for comparative studies was 15 ± 1.5 (4 studies), indicating that the comparative studies were fair in quality (Table I). Most of the studies had a clearly stated aim, endpoints appropriate to the study aim, and follow-up periods appropriate to the study aim. However, many studies failed to report or perform an unbiased assessment of the study endpoints, as well as prospectively calculate the study size. Considerable loss to follow-up owing to patient deaths was also frequently observed. The comparative studies had appropriate and contemporary control groups and good baseline equivalence between study and control groups but lacked in statistical analysis as they did not report 95% CIs or relative risks (Appendix S2).

Table I Classification of HO

	Data
Hasting and Graham classification	
Celli and Bonucci[12]	4 class I or IIa, 0 class III
Celli[11]	2 class I or IIa, 0 class III
Kodde et al[27]	7 class I, 1 class II, 0 class III
Brooker classification	
Brinkman et al[9]	9 class I, 5 class II, 0 class III
McKee et al[34]	0 class I, 0 class II, 3 class III
Custom classification	
Bai et al[4]	36% grade 1, 47% grade 2, 15% grade 3

HO, heterotopic ossification.

Table II Summary of HO by indication for TEA

Diagnosis	No. of studies	No. of TEA patients	No. of HO patients (%)	No. of symptomatic HO patients (%)	No. of HO patients undergoing revision (%)
Rheumatoid arthritis	12	371	24 (6.5)	5 (1.3)	2 (0.5)
Distal humeral fracture	11	330	56 (17.0)	9 (2.7)	1 (0.3)
Fracture nonunion	4	123	10 (8.1)	1 (0.8)	1 (0.8)
Post-traumatic arthritis	3	108	5 (4.6)	4 (3.7)	3 (2.8)
Ankylosis	2	29	8 (27.6)	2 (6.9)	1 (3.4)
Primary osteoarthritis	2	19	4 (21.1)	1 (5.3)	0 (0.0)
Fracture malunion	1	20	4 (20.0)	0 (0.0)	0 (0.0)
Revision	1	17	4 (23.5)	0 (0.0)	0 (0.0)
Complex elbow fracture	1	2	0 (0.0)	0 (0.0)	0 (0.0)
Tumor resection	1	1	0 (0.0)	0 (0.0)	0 (0.0)
Overall	31	1020	115 (11.3)	22 (2.2)	8 (0.8)

HO, heterotopic ossification; *TEA*, total elbow arthroplasty.

Classifications

HO classification was reported in 7 studies (n = 226). The Hasting and Graham HO classification system was used in 3 studies (n = 52).[11,12,27] HO was classified as follows: I, subclinical; IIa, limits flexion and extension; IIb, limits pronation and supination; IIc, limits motion in both planes; or III, complete ankylosis.[20] Two studies classified 6 HO patients as either class I or IIa.[11,12] Kodde et al[27] identified 9 HO patients as class I and 1 HO patient as class IIa.

The Brooker classification system, originally used to classify HO after THA, was applied in 2 studies.[9,34] The original classification system was defined as: I, islands of bone within the soft tissues about the hip; II, bone spurs from the pelvis or proximal end of the femur, leaving at least 1 cm between opposing bone surfaces; III, bone spurs from the pelvis or proximal end of the femur, reducing the space between opposing bone surfaces to less than 1 cm; and IV, apparent bone ankylosis of the hip.[10] Brinkman et al[9] found 9 elbows to be Brooker class I and 5 elbows to be Brooker class II. McKee et al[34] classified 3 patients as Brooker class III.

Besides these 2 classification systems, Bai et al[4] used a custom classification system for the degree of HO defined as follows: 0, no HO; 1, mild HO; 2, formation of near ankylosing HO between 2 surfaces; or 3, ankylosis of HO between 2 surfaces. With these criteria, 36% of HO elbows were classified as grade 1; 47%, grade 2; and 15%, grade 3.[4] Figgie et al[18] only stated that all HO patients were grade I without further specifying the classification criteria used, and this study was therefore not included in the summary table (Table I).

Symptoms

Several symptoms were reported in the included studies, including limited ROM, ankylosis, pain, and swelling. Overall, 59 of the 233 HO patients (2.6%) were found to be symptomatic. By use of information from 31 studies (n = 1020), symptomatic HO developed after TEA in 2 of 29 ankylosis patients (7%), 1 of 19 primary osteoarthritis patients (5%), 4 of 108 post-traumatic arthritis patients (4%), 9 of 330 distal humeral fracture patients (3%), 5 of 371 rheumatoid arthritis patients (1%), and 1 of 123 fracture nonunion patients (1%) (Table II).

Risk factors

Indication for TEA

Thirty-one studies reported the indication (n = 1020) for both patients who underwent TEA and those in whom HO developed postoperatively. HO developed after TEA in 8 of 29 ankylosis patients (24%), 2 of 19 primary osteoarthritis patients (21%), 56 of 330 distal humeral fracture patients (17%), 4 of 123 fracture nonunion patients (8%), 24 of 371 rheumatoid arthritis patients (6%), and 3 of 108 post-traumatic arthritis patients (5%) (Table II).

Prosthesis

The type of implant used in both TEA patients and those in whom HO developed was reported in 41 studies (n = 2115). HO developed after TEA in 110 of 1602 patients (7%) with Coonrad or Coonrad-Morrey implants, 0 of 40 patients (0%) with Souter-Strathclyde implants, and 24 of 139 patients (17%) with Kudo implants (Table III).

Obesity

Using data from 723 TEAs in 654 patients, Baghdadi et al[3] found that HO was more likely to develop after TEA in obese patients. HO developed in 16 of 159 TEAs (10%) for obese patients, whereas the complication developed in only 16 of 564 TEAs (3%) for non-obese patients. Body mass index (BMI) was obtained preoperatively, and patients with BMI of 30 kg/m^2 or greater were classified as obese. A significant difference ($P < .05$) in the average BMI was found between patients with inflammatory conditions (25 ± 5 kg/m^2) and those with traumatic conditions (28 ± 6 kg/m^2).[3]

Table III HO by type of prosthesis

Implant	No. of studies	No. of TEA patients	No. of HO patients	% HO patients
Coonrad/ Coonrad-Morrey (Zimmer, Warsaw, IN, USA)	30	1602	110	6.9
Kudo (Biomet UK Ltd, Swindon, UK)	4	139	24	17.3
Semiconstrained*	1	102	50	49
Roper-Tuke	1	59	1	1.7
Latitude (Wright, Memphis, TN, USA)	1	58	1	1.7
BiContact (Impol, São Paulo, Brazil)	1	45	1	2.2
Baksi	1	41	2	4.9
Souter-Strathclyde (Stryker Howmedica Osteonics, Limerick, Ireland)	1	40	0	0.0
Solar (Stryker, Kalamazoo, MI, USA)	1	23	1	4.3
Capitellocondylar (DePuy, Warsaw, IN, USA)	1	6	1	16.7
Overall	41	2115	191	9.0

HO, heterotopic ossification; *TEA*, total elbow arthroplasty.
* Study reported implant as semiconstrained without further specifications.

Management

The treatment of HO after TEA was reported in 14 studies, which described the management of 15 patients with HO. In total, 13 patients (0.6%) underwent surgical intervention because of HO. This included resection and/or excision in 10 patients, contracture release in 1 patient, and revision surgery not further specified in 2 patients. Oral indomethacin was administered alone in 1 patient; combined with surgical resection, prednisolone, and etidronate disodium in 1 patient; and combined with surgical resection and radiotherapy (single dose, 700 cGy) in 1 patient. Three patients undergoing surgical intervention for HO had an arc of motion greater than or equal to 100° and one had a 65° arc of motion postoperatively. One patient undergoing surgical intervention had an excellent Mayo Elbow Performance Score (MEPS) and two had a good MEPS postoperatively. The progression of HO stopped in 1 patient, who had been given indomethacin. No recurrence of HO was reported in the resected patients. In total, outcomes after management were reported in 6 studies including 6 treated HO patients (Table IV).

Analysis by diagnosis using information from 31 studies (n = 1020) showed that 1 of 29 ankylosis patients (3%), 3 of 108 post-traumatic arthritis patients (3%), 1 of 123 fracture nonunion patients (1%), 2 of 371 rheumatoid arthritis patients (0.5%), and 1 of 330 distal humeral fracture patients (0.3%) underwent surgical intervention for HO after TEA (Table II).

Prophylactic measures

Most of the included studies did not report whether prophylactic measures were used to prevent the formation of HO. Two studies reported that prophylactic measures were not routinely used.[47,54] One study administered single-beam external radiation between 600 and 800 cGy in 4 patients with moderate to severe HO preoperatively to prevent its recurrence.[40] Of the 4 patients, 1 also received indomethacin for 8 weeks. Nevertheless, HO developed postoperatively in 3 patients (75%), leading to surgical resection of HO in 1 case. The resected patient had an excellent MEPS (100) with ROM of 25° to 140°. Two patients rated their condition as "worse" because of restricted movement but declined surgery to excise the ectopic bone.[40] In another study, perioperative indomethacin was administered to a patient with a previous head injury and preoperative elbow ankylosis.[37] However, HO still developed postoperatively in the patient, leading to surgical resection.[37] Overall, HO developed in 4 of 5 patients (80%) who received prophylactic measures.

Discussion

Despite numerous studies reporting the incidence of HO after hip and knee arthroplasties, the incidence of HO after TEA is sparsely reported in the literature. In this systematic review, the incidence of HO was estimated to be around 10% after averaging of data from 45 studies including 2256 TEA patients. This rate is considerably lower than the incidence of HO after THA, which was reported to be 47% by Kocic et al.[26] There was considerable variance in the incidence of HO among studies, ranging from 1% to 57%, excluding 1 case report that had an incidence rate of 100%. This highly variable rate could be attributed to different surgical techniques, follow-up times, and definitions of HO to meet criteria and varying predisposing factors in patients among studies.

Of the 10% of HO patients, 25% (3% overall) were reported to be symptomatic and only 6% (0.6% overall) received surgical intervention because of HO. This finding is important as it indicates that HO is a relatively uncommon complication of TEA, with most patients being asymptomatic and very few requiring surgical management. Surgical resection was the most popular method of management for symptomatic HO patients and led to a good arc of motion and MEPS outcomes in reported patients. This finding was in agreement with the results of Salazar et al,[45] who found that surgical excision led to an improvement in the mean flexion-extension arc of motion from 35° to 103° ($P < .001$; 95% CI, 57°-80°) in 39 patients (46 elbows) with HO of the elbow. In addition, no recurrence of HO was reported after resection. Oral indomethacin alone was administered in 1 case, which stopped further progression of HO.[50] Indomethacin and

Table IV Management and outcome after management of HO

Studies	Management	Outcome after management
Aldridge et al[1]	Resection of HO ($n_{HO} = 1$)	Good MEPS rating
Allen and Nunley[2]	Excision of HO, postoperative radiation therapy (single dose, 700 cGy), and indomethacin ($n_{HO} = 1$)	Patient had ROM of 0°-120° and 80° for pronation-supination and no recurrence of HO
Bai et al[4]	Excised painful HO ($n_{HO} = 1$)	NR
Benegas et al[6]	Revision surgery because of HO but did not further specify operation ($n_{HO} = 1$)	NR
Boorman et al[8]	Repeat surgery because of excessive stiffness due to HO but did not further specify operation ($n_{HO} = 1$)	NR
Cil et al[13]	Excision of HO and anconeus triceps-plasty because of triceps insufficiency ($n_{HO} = 1$)	NR
Kudo et al[29]	Reoperation to remove fibrous scar tissue and ectopic bone followed by administration of prednisolone, etidronate disodium, and indomethacin ($n_{HO} = 1$)	Postoperative ROM was from 65° to 125° with MEPS of 85 (good) compared with preoperative ROM of 60°-80° with MEPS of 35
Linn et al[31]	Contracture release ($n_{HO} = 1$)	ROM was 30°-130°
McKee et al[34]	Resection of HO and revision of ulnar nerve transposition ($n_{HO} = 1$)	MEPS was 100 (excellent); ROM was from 24° to 140°
Oizumi et al[38]	Excision 1 yr after TEA ($n_{HO} = 1$)	NR
Peden and Morrey[40]	Resection of HO ($n_{HO} = 1$)	NR
Throckmorton et al[49]	Resection of HO ($n_{HO} = 2$)	NR
Tian et al[50]	Oral administration of indomethacin ($n_{HO} = 1$)	Did not progress after administration of indomethacin and hardly influenced activities
Toulemonde et al[51]	Resection of HO ($n_{HO} = 1$)	NR
Summary		
Surgery only		n = 11
Surgery, indomethacin, prednisolone, and etidronate disodium		n = 1
Surgery, indomethacin, and radiotherapy		n = 1
Indomethacin only		n = 1
Total		n = 14

HO, heterotopic ossification; n_{HO}, number of HO patients treated; *MEPS*, Mayo Elbow Performance Score; *ROM*, range of motion; *NR*, not reported.

radiotherapy were used to prevent the recurrence of HO after resection in 2 cases.[2,29]

This review also conducted preliminary investigation into the risk factors that affect the incidence of HO. Baghdadi et al[3] reported that obese patients were at higher risk of HO development than non-obese patients. However, no BMI information was available for the other included studies. Thus, it was unknown whether obesity was also a predisposing factor in other studies. Analysis of 31 studies (n = 1020) found that symptomatic HO was more likely to develop in patients with preoperative ankylosis, primary osteoarthritis, and post-traumatic arthritis. This conclusion agrees with the results of Zhu et al,[58] who found ankylosing spondylitis (odds ratio [OR], 1.90; 95% CI, 1.07-3.37) and an ankylosed hip (OR, 9.85; 95% CI, 2.61-37.24) to be risk factors for HO after THA. Because of the high incidence of HO in patients with preoperative ankylosis, it would likely be beneficial for high-risk patients to receive prophylactic treatment to prevent the formation of HO.

In this review, perioperative prophylaxis using indomethacin and/or radiotherapy was administered to 5 high-risk patients in 2 studies and did not appear to be effective in either study. HO developed after TEA in 4 of 5 treated patients (80%). This finding was contradictory to the known effectiveness of HO prophylaxis for other surgical procedures. For instance, a recent systematic review and meta-analysis by Kan et al[23] found a significant decrease in the incidence of HO after prophylactic therapy using NSAIDs according to both the Brooker scale (OR, 2.8; 95% CI, 1.9-4.0) and Delee scale (OR, 10.0; 95% CI, 5.6-16.2). Another systematic review comparing radiotherapy versus NSAIDs found both were equally effective at preventing HO.[53] A possible explanation for the disparity in results is that because HO prophylaxis was so rarely reported for TEA, it was at a high risk of selection bias in which authors were more likely to report instances in which the prophylaxis was not effective. Nevertheless, because HO is an uncommon complication of TEA and symptomatic HO is even more uncommon, routine HO prophylaxis for TEA is unwarranted. However, prophylaxis could be helpful for high-risk patients with previous ankylosis. For those patients, further studies are needed to more systematically investigate the effectiveness of prophylaxis to determine whether it would be useful in reducing the incidence of HO.

Strengths and limitations

This review was strengthened by a rigorous methodology. All screening and data extraction were completed by 2 independent reviewers, with substantial inter-reviewer agreement at

all stages. In total, our review included 2256 TEA patients and 233 HO patients. The large sample size allowed us to summarize predisposing factors and investigate potential risk factors.

However, the strength of the conclusions derived from this systematic review is limited by the quality of the included studies. Most studies were retrospective observational studies that investigated the outcomes of TEA patients. The studies did not directly focus on HO patients and offered limited information on the demographic characteristics, predisposing factors, functional outcomes, pain, diagnoses, and management of the HO patients. Often, 1 or more of these outcomes of interest were not reported by the study or it was not possible to isolate information regarding the HO patients from other TEA patients. A classification system was used in only 7 of the included studies, which made it difficult to objectively review the severity of the symptoms. Prophylaxis was not consistently used or reported, which hampered the validity of derived conclusions owing to selection bias. Although 4 studies were excluded in this review because of definitive overlap in included patients, there were also some retrospective observational studies conducted at the same institution in which the overlap between reported patients was unclear, in which case both studies were included. Moreover, there was a high degree of heterogeneity between and within the included studies, such as using a wide range of techniques and implants and including patients with different indications for surgery without specifying the information for each individual patient. This could be partly attributed to the fact that TEA was still a relatively uncommon procedure and heterogeneous patients were included to increase the sample size. Finally, because the procedure was commonly performed in an older population, loss of follow-up because of deaths was a problem encountered in most included studies.

In addition, the incidence of HO could have been overestimated owing to selective inclusion of studies in this review, which only included TEA studies in which HO developed postoperatively in at least 1 patient. This meant that any TEA studies in which 0 patients had HO development were not included, leading to an overestimation of HO patients.

Conclusion

HO appears to be an uncommon complication after TEA, with most HO patients being asymptomatic and requiring no management. Surgical management results in good to excellent outcomes in the arc of motion and MEPS in reported patients. HO develops in a higher percentage of patients undergoing TEA because of ankylosis, primary osteoarthritis, and distal humeral fractures. It is interesting to note that a higher percentage of patients in whom HO developed after TEA performed for ankylosis and post-traumatic osteoarthritis later required surgical intervention for the complication. The effectiveness of prophylaxis in high-risk patients is uncertain, and future studies are needed to clarify its usefulness. The strength of these conclusions is limited by inconsistent reporting in the available literature.

Disclaimer

The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jse.2018.10.003

References

1. Aldridge JM, Lightdale NR, Mallon WJ, Coonrad RW. Total elbow arthroplasty with the Coonrad/Coonrad-Morrey prosthesis: a 10-to 31-year survival analysis. J Bone Joint Surg Br 2006;88:509-14. http://dx.doi.org/10.1302/0301-620X.88B4.17095
2. Allen DM, Nunley JA Jr. Heterotopic ossification complicating total elbow replacement in a patient with rheumatoid arthritis. J South Orthop Assoc 1999;8:101-4.
3. Baghdadi YM, Veillette CJ, Malone AA, Morrey BF, Sanchez-Sotelo J. Total elbow arthroplasty in obese patients. J Bone Joint Surg Am 2014;96:e70. http://dx.doi.org/10.2106/JBJS.M.00364
4. Bai XS, Petscavage-Thomas JM, Ha AS. Total elbow arthroplasty: a radiographic outcome study. Skeletal Radiol 2016;45:789-94. http://dx.doi.org/10.1007/s00256-016-2351-5
5. Baksi DP, Pal AK, Baksi D. Prosthetic replacement of elbow for intercondylar fractures (recent or ununited) of humerus in the elderly. Int Orthop 2011;35:1171-7. http://dx.doi.org/10.1007/s00264-010-1122-5
6. Benegas E, Malavolta EA, Gracitelli ME, Sousa AT, Miyazaki AN, Fregoneze M, et al. Results from Bi-Contact® total elbow arthroplasty: multicenter study. Rev Bras Ortop 2011;46:565-71. http://dx.doi.org/10.1016/S2255-497115)30413-4
7. Blaine TA, Adams R, Morrey BF. Total elbow arthroplasty after interposition arthroplasty for elbow arthritis. J Bone Joint Surg Am 2005;87:286-92. http://dx.doi.org/10.2106/JBJS.03031pp
8. Boorman RS, Page WT, Weldon EJ III, Lippitt S, Matsen FA III. A triceps-on approach to semi-constrained total elbow arthroplasty. Tech Shoulder Elbow Surg 2003;4:139-44.
9. Brinkman JM, De Vos MJ, Eygendaal D. Failure mechanisms in uncemented Kudo type 5 elbow prosthesis in patients with rheumatoid arthritis: 7 of 49 ulnar components revised because of loosening after 2-10 years. Acta Orthop 2007;78:263-70. http://dx.doi.org/10.1080/17453670710013780
10. Brooker AF, Bowerman JW, Robinson RA, Riley LH Jr. Ectopic ossification following total hip replacement: incidence and a method of classification. J Bone Joint Surg Am 1973;55:1629-32.
11. Celli A. A new posterior triceps approach for total elbow arthroplasty in patients with osteoarthritis secondary to fracture: preliminary clinical experience. J Shoulder Elbow Surg 2016;25:e223-31. http://dx.doi.org/10.1016/j.jse.2016.04.003

12. Celli A, Bonucci P. The anconeus–triceps lateral flap approach for total elbow arthroplasty in rheumatoid arthritis. Musculoskelet Surg 2016;100:73-83. http://dx.doi.org/10.1007/s12306-016-0417-0
13. Cil A, Veillette CJ, Sanchez-Sotelo J, Morrey BF. Linked elbow replacement: a salvage procedure for distal humeral nonunion. J Bone Joint Surg Am 2008;90:1939-50. http://dx.doi.org/10.2106/JBJS.G.00690
14. Dos Remedios C, Chantelot C, Giraud F, Migaud H, Fontaine C. Results with Kudo elbow prostheses in non-traumatic indications: a study of 36 cases. Acta Orthop Belg 2005;71:273-88.
15. Dryer RF, Buckwalter JA, Sprague BL. Hinged total elbow replacement. Orthopedics 1981;4:763-8.
16. Ducrot G, Ehlinger M, Adam P, Di Marco A, Clavert P, Bonnomet F. Complex fractures of the distal humerus in the elderly: is primary total elbow arthroplasty a valid treatment alternative? A series of 20 cases. Orthop Traumatol Surg Res 2013;99:10-20. http://dx.doi.org/10.1016/j.otsr.2012.10.010
17. Figgie MP, Inglis AE, Mow CS. Salvage of non-union of supracondylar fracture of the humerus by total elbow arthroplasty. J Bone Joint Surg Am 1989;71:1058-65.
18. Figgie MP, Inglis AE, Mow CS. Total elbow arthroplasty for complete ankylosis of the elbow. J Bone Joint Surg Am 1989;71:513-20.
19. Gambirasio R, Riand N, Stern R, Hoffmeyer P. Total elbow replacement for complex fractures of the distal humerus: an option for the elderly patient. J Bone Joint Surg Br 2001;83:974-8.
20. Graham TJ. The classification and treatment of heterotopic ossification about the elbow and forearm. Hand Clin 1994;10:417-37.
21. Hildebrand KA, Patterson SD, Regan WD, MacDermid JC, King GJ. Functional outcome of semiconstrained total elbow arthroplasty. J Bone Joint Surg Am 2000;82:1379.
22. Kamineni S, Morrey BF. Distal humeral fractures treated with noncustom total elbow replacement. J Bone Joint Surg Am 2004;86:940-7.
23. Kan SL, Yang B, Ning GZ, Chen LX, Li YL, Gao SJ, et al. Nonsteroidal anti-inflammatory drugs as prophylaxis for heterotopic ossification after total hip arthroplasty: a systematic review and meta-analysis. Medicine (Baltimore) 2015;94:e828. http://dx.doi.org/10.1097/MD.0000000000000828
24. King GJ, Adams RA, Morrey BF. Total elbow arthroplasty: revision with use of a non-custom semiconstrained prosthesis. J Bone Joint Surg Am 1997;79:394-400.
25. Kiran M, Jariwala A, Wigderowitz C. Medium term outcomes of primary and revision Coonrad-Morrey total elbow replacement. Indian J Orthop 2015;49:233. http://dx.doi.org/10.4103/0019-5413.152497
26. Kocic M, Lazovic M, Mitkovic M, Djokic B. Clinical significance of the heterotopic ossification after total hip arthroplasty. Orthopedics 2010;33:16. http://dx.doi.org/10.3928/01477447-20091124-13
27. Kodde IF, van Riet RP, Eygendaal D. Semiconstrained total elbow arthroplasty for posttraumatic arthritis or deformities of the elbow: a prospective study. J Hand Surg Am 2013;38:1377-82. http://dx.doi.org/10.1016/j.jhsa.2013.03.051
28. Kudo H, Iwano K. Total elbow arthroplasty with a non-constrained surface-replacement prosthesis in patients who have rheumatoid arthritis. A long-term follow-up study. J Bone Joint Surg Am 1990;72:355-62.
29. Kudo H, Iwano K, Nishino J. Total elbow arthroplasty with use of a nonconstrained humeral component inserted without cement in patients who have rheumatoid arthritis. J Bone Joint Surg Am 1999;81:1268-80.
30. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74.
31. Linn MS, Gardner MJ, McAndrew CM, Gallagher B, Ricci WM. Is primary total elbow arthroplasty safe for the treatment of open intra-articular distal humerus fractures? Injury 2014;45:1747-51. http://dx.doi.org/10.1016/j.injury.2014.07.017
32. Little CP, Graham AJ, Carr AJ. Total elbow arthroplasty: a systematic review of the literature in the English language until the end of 2003. J Bone Joint Surg Br 2005;87:437-44. http://dx.doi.org/10.1302/0301-620X.87B4.15692
33. Maheshwari R, Vaziri S, Helm RH. Total elbow replacement with the Coonrad-Morrey prosthesis: our medium to long-term results. Ann R Coll Surg Engl 2012;94:189-92. http://dx.doi.org/10.1308/003588412X13171221589775
34. McKee MD, Veillette CJ, Hall JA, Schemitsch EH, Wild LM, McCormack R, et al. A multicenter, prospective, randomized, controlled trial of open reduction—internal fixation versus total elbow arthroplasty for displaced intra-articular distal humeral fractures in elderly patients. J Shoulder Elbow Surg 2009;18:3-12. http://dx.doi.org/10.1016/j.jse.2008.06.005
35. Mehta SS, Watts AC, Talwalkar SC, Birch A, Nuttall D, Trail IA. Early results of Latitude primary total elbow replacement with a minimum follow-up of 2 years. J Shoulder Elbow Surg 2017;26:1867-72. http://dx.doi.org/10.1016/j.jse.2017.06.037
36. Muller LP, Kamineni S, Rommens PM, Morrey BF. Primary total elbow replacement for fractures of the distal humerus. Oper Orthop Traumatol 2005;17:119-42. https://doi.org/10.1007/s00064-005-1125-3
37. Obert L, Ferrier M, Jacquot A, Mansat P, Sirveaux F, Clavert P, et al. Distal humerus fractures in patients over 65: complications. Orthop Traumatol Surg Res 2013;99:909-13. http://dx.doi.org/10.1016/j.otsr.2013.10.002
38. Oizumi N, Suenaga N, Yoshioka C, Yamane S. Triceps-sparing ulnar approach for total elbow arthroplasty. Bone Joint J 2015;97:1096-101. http://dx.doi.org/10.1302/0301-620X.97B8.34956
39. Pai VS. Heterotopic ossification in total hip arthroplasty: the influence of the approach. J Arthroplasty 1994;9:199-202.
40. Peden JP, Morrey BF. Total elbow replacement for the management of the ankylosed or fused elbow. J Bone Joint Surg Br 2008;90:1198-204. http://dx.doi.org/10.1302/0301-620X.90B9.19967
41. Prasad N, Ali A, Stanley D. Total elbow arthroplasty for non-rheumatoid patients with a fracture of the distal humerus: a minimum ten-year follow-up. Bone Joint J 2016;98:381-6. http://dx.doi.org/10.1302/0301-620X.98B3.35508
42. Prasad N, Dent C. Outcome of total elbow replacement for rheumatoid arthritis: single surgeon's series with Souter-Strathclyde and Coonrad-Morrey prosthesis. J Shoulder Elbow Surg 2010;19:376-83. http://dx.doi.org/10.1016/j.jse.2009.09.016
43. Prasad N, Dent C. Outcome of total elbow replacement for distal humeral fractures in the elderly: a comparison of primary surgery and surgery after failed internal fixation or conservative treatment. J Bone Joint Surg Br 2008;90:343-8. http://dx.doi.org/10.1302/0301-620X.90B3.18971
44. Prkić A, van Bergen CJ, The B, Eygendaal D. Total elbow arthroplasty is moving forward: review on past, present and future. World J Orthop 2016;7:44. http://dx.doi.org/10.5312/wjo.v7.i1.44
45. Salazar D, Golz A, Israel H, Marra G. Heterotopic ossification of the elbow treated with surgical resection: risk factors, bony ankylosis, and complications. Clin Orthop Relat Res 2014;472:2269-75. http://dx.doi.org/10.1007/s11999-014-3591-0
46. Schneeberger AG, Adams R, Morrey BF. Semiconstrained total elbow replacement for the treatment of post-traumatic osteoarthrosis. J Bone Joint Surg Am 1997;79:1211-22.
47. Schoch BS, Werthel JD, Sánchez-Sotelo J, Morrey BF, Morrey M. Total elbow arthroplasty for primary osteoarthritis. J Shoulder Elbow Surg 2017;26:1355-9. http://dx.doi.org/10.1016/j.jse.2017.04.003
48. Shehab D, Elgazzar AH, Collier BD. Heterotopic ossification. J Nucl Med 2002;43:346-53.
49. Throckmorton T, Zarkadas P, Sanchez-Sotelo J, Morrey B. Failure patterns after linked semiconstrained total elbow arthroplasty for posttraumatic arthritis. J Bone Joint Surg Am 2010;92:1432-41. http://dx.doi.org/10.2106/JBJS.I.00145
50. Tian W, He C, Jia J. Total elbow joint replacement for the treatment of distal humerus fracture of type c in eight elderly patients. Int J Clin Exp Med 2015;8:10066.
51. Toulemonde J, Ancelin D, Azoulay V, Bonnevialle N, Rongières M, Mansat P. Complications and revisions after semi-constrained total elbow arthroplasty: a mono-centre analysis of one hundred cases. Int Orthop 2016;40:73-80. http://dx.doi.org/10.1007/s00264-015-3008-z

52. Trepman E, Vella IM, Ewald FC. Radial head replacement in capitellocondylar total elbow arthroplasty: 2-to 6-year follow-up evaluation in rheumatoid arthritis. J Arthroplasty 1991;6:67-77.
53. Vavken P, Castellani L, Sculco TP. Prophylaxis of heterotopic ossification of the hip: systematic review and meta-analysis. Clin Orthop Relat Res 2009;467:3283. http://dx.doi.org/10.1007/s11999-009-0924-5
54. Viveen J, Prkic A, Koenraadt KL, Kodde IF, Eygendaal D. Clinical and radiographic outcome of revision surgery of total elbow prosthesis: midterm results in 19 cases. J Shoulder Elbow Surg 2017;26:716-22. http://dx.doi.org/10.1016/j.jse.2016.10.010
55. Welsink CL, Lambers KT, van Deurzen DF, Eygendaal D, van den Bekerom MP. Total elbow arthroplasty: a systematic review. JBJS Rev 2017;5:e4. http://dx.doi.org/10.2106/JBJS.RVW.16.00089
56. Willems K, De Smet L. The Kudo total elbow arthroplasty in patients with rheumatoid arthritis. J Shoulder Elbow Surg 2004;13:542-7. https://doi.org/10.1016/j.jse.2004.02.017
57. Yanni ON, Fearn CB, Gallannaugh SC, Joshi R. The Roper-Tuke total elbow arthroplasty. 4- to 10-year results of an unconstrained prosthesis. J Bone Joint Surg Br 2000;82:705-10.
58. Zhu Y, Zhang F, Chen W, Zhang Q, Liu S, Zhang Y. Incidence and risk factors for heterotopic ossification after total hip arthroplasty: a meta-analysis. Arch Orthop Trauma Surg 2015;135:1307-14. http://dx.doi.org/10.1007/s00402-015-2277-8