

The use of intramedullary devices for adult radial head and neck fractures. A systematic review

Robert JORDAN¹, Mohammed REMTULLA¹, Alistair JONES², Shahbaz MALIK³, Samuel CHAN¹, Gunaratnam SHYAMALAN¹

¹University Hospitals Birmingham, England; ²Taunton Hospital, England; ³Worcestershire Acute Hospital NHS Trust, England.

Correspondence at: R W Jordan, University Hospitals Birmingham, Birmingham, B15 2WB, England, Email: Robert.jordan@doctors.org.uk

The management of isolated radial neck and head fractures is controversial. Plate fixation and tripod fixation are two commonly employed techniques but risk damage to soft tissues and implant-related complications. Intramedullary fixation is commonly used in pediatric cases and reduces the potential drawbacks of open fixation. This systematic review aimed to analyze outcomes of intramedullary fixation in adults in terms of function, union, and complication rates. A systematic review of the literature was conducted following the PRISMA guidelines using Medline and EMBASE's online databases. The review was registered on the PROSPERO database. Studies were appraised using the Methodological Index for non-randomized studies (MINORS) tool. Seven studies were deemed eligible for inclusion (n=55). Mean ages of patients ranged from 31.3 to 44.2 years, and mean follow-up ranged from 9 to 86 months. The Mayo Elbow Performance score (MEPs) was reported in five case series (mean scores 81.8 -97.9) and the prevalence of excellent results ranged from 71% and 83%. Although 100% of fractures united, the pooled complication rate was 24% (range 0-50%). The most common complications were elbow stiffness (7%), superficial radial nerve neuropraxia (7%), malunion (5%), and AVN (1.8%). No study reported any patients requiring revision surgery. Intramedullary fixation for radial head and neck fractures appears to provide a reliable alternative treatment option in terms of union, range of motion, and functional outcomes. Further robust trials direct comparing against open fixation techniques are required.

Keywords: Radial head fracture, radial neck fracture, intramedullary fixation, titanium elastic nails.

INTRODUCTION

Isolated radial neck fractures in adults are very rare, with an incidence of 1% of all fractures¹. The mechanism of injury is commonly a fall onto an extended and supinated forearm. Management of isolated radial neck fractures is controversial². Non-displaced fractures may be treated conservatively with early elbow mobilization to avoid stiffness^{3,4}. Displaced fractures in adults tend to be managed surgically as the remodelling of these fractures is limited, and malunion can cause restriction in motion^{5,6}. Open reduction and internal fixation using locked plating are recommended treatment options⁵ and are reliable even in complex fracture patterns⁷. The tripod technique using headless compression screws has recently been advocated⁸ with biomechanical studies and early clinical results suggesting comparable results to plate fixation^{9,10}. However, both techniques require dissection of the radial head and periosteal stripping, which carries the risk of devascularisation of the radial head and implant-related complications¹¹⁻¹⁴.

Intramedullary fixation of radial head and neck fractures is a commonly reported technique for

managing paediatric displaced radial neck fractures^{15,16}. This technique is attractive as it reduces the risk of radial head necrosis, non-union, heterotopic ossification, and restricted forearm motion¹⁷. However, limited literature is available to support using an intramedullary device to fix radial neck and head fractures in adults. This systematic review aimed to analyze the outcome of intramedullary fixation of the radial neck and head fractures in adults regarding function, union, and complication rates.

PATIENT AND METHODS

A systematic review of the literature was conducted in accordance with the PRISMA guidelines¹⁸ using the online databases Medline and EMBASE. The study was registered on the PROSPERO database. The searches were performed independently by two authors on the 25th of January 2021 and repeated on the 1st of February 2021 to ensure accuracy. Search terms included 'radial neck fracture' and 'intramedullary fixation.' Any discrepancies were resolved through

Table I. — Methodological items for non-randomized studies (MINORS) Score.

	Singh et al. ²⁰	Kaziz et al. ²¹	Keller et al. ²²	Bushu et al. ²³	Gao et al. ²⁴	Sandmann et al. ²⁶
A clearly stated aim: the question addressed should be precise and relevant in the light of available literature	2	2	2	2	2	2
Inclusion of consecutive patients: all patients potentially fit for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion or details about the reasons for exclusion)	2	0	0	0	2	2
Prospective collection of data: data were collected according to a protocol established before the beginning of the study	2	1	1	1	1	1
Endpoints appropriate to the aim of the study: unambiguous explanation of the criteria used to evaluate the main outcome which should be in accordance with the question addressed by the study. Also, the endpoints should be assessed on an intention-to-treat basis.	2	2	2	2	2	2
Unbiased assessment of the study endpoint: blind evaluation of objective endpoints and double-blind evaluation of subjective endpoints. Otherwise the reasons for not blinding should be stated	0	0	0	0	2	2
Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events	2	2	2	2	2	2
Loss to follow up less than 5%: all patients should be included in the follow up. Otherwise, the proportion lost to follow up should not exceed the proportion experiencing the major endpoint	1	2	2	2	2	1
Prospective calculation of the study size: information of the size of detectable difference of interest with a calculation of 95% confidence interval, according to the expected incidence of the outcome event, and information about the level for statistical significance and estimates of power when comparing the outcomes	N/A	N/A	N/A	N/A	N/A	N/A
An adequate control group: having a gold standard diagnostic test or therapeutic intervention recognized as the optimal intervention according to the available published data	N/A	N/A	N/A	N/A	N/A	N/A
Contemporary groups: control and studied group should be managed during the same time period (no historical comparison)	N/A	N/A	N/A	N/A	N/A	N/A
Baseline equivalence of groups: the groups should be similar regarding the criteria other than the studied endpoints. Absence of confounding factors that could bias the interpretation of the results	N/A	N/A	N/A	N/A	N/A	N/A
Adequate statistical analyses: whether the statistics were in accordance with the type of study with calculation of confidence intervals or relative risk	1	1	1	1	1	1
Total	12	10	10	10	14	13

The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score being 16 for non-comparative studies.

discussion between these two authors, with the senior author resolving any residual differences.

The eligibility criteria were clinical studies published in English that reported on adult patients (over 15 years of age) managed surgically for radial head or neck fractures using an intramedullary device. Any type of intramedullary device was permitted, including the use of additional K-wires to aid reduction. The studies were required to report either functional outcome, union or complication rates during follow-up for inclusion. Only primary research was considered for review, with any abstracts, comments, review, biomechanical and technique articles excluded. The clinical studies were appraised independently by two authors, and quality assessment of non-randomized studies was completed using the Methodological Index for non-randomised studies (MINORS) tool¹⁹ MINORS is a validated scoring tool for non-randomized studies. Each of the 8 items in the MINORS criteria relevant to the case series was given a score of 0, 1, or 2, with a maximum score of 16 (Table I).

RESULTS

The search strategy is illustrated in Figure 1 and identified 34 studies for consideration. After application of inclusion criteria, seven studies were deemed eligible for inclusion (n=55)²⁰⁻²⁶. Singh et al.²⁰ reported a prospective case series, five further studies were retrospective case series²¹⁻²⁵ and Serbest et al. reported a case report⁶. Concise study characteristics are summarised in Table II. The mean ages of patients in the included studies ranged from 31.3 to 44.2 years, and the mean follow-up ranged from 9 to 86 months. The studies included a variety of fracture patterns from Mason I to III fractures, and Gao et al.²⁴ reported on partial articular radial head fractures. Three studies used an intramedullary Kirschner wire ranging from 1.6mm to 3mm^{21,22,26}, whilst the remainder used titanium elastic nails (TENS)^{20,23,24,25}.

Five case series reported functional outcomes^{20,21,23-25}; the Mayo Elbow Performance score (MEPs) was the most reported in all five, and the mean scores ranged from 81.8 to 97.9. Three studies described the prevalence of excellent results, which ranged between 71% and 83% of patients²³⁻²⁵. Three case series reported function using the Quick DASH score with the mean scores ranging from 2.33 to 6.81.

Five case series reported a range of motion post-operatively²⁰⁻²⁴. Bushu et al.²³ managed Mason type III fractures and reported a mean flexion arc of 142.5 degrees, mean pronation of 96.25 degrees, and mean

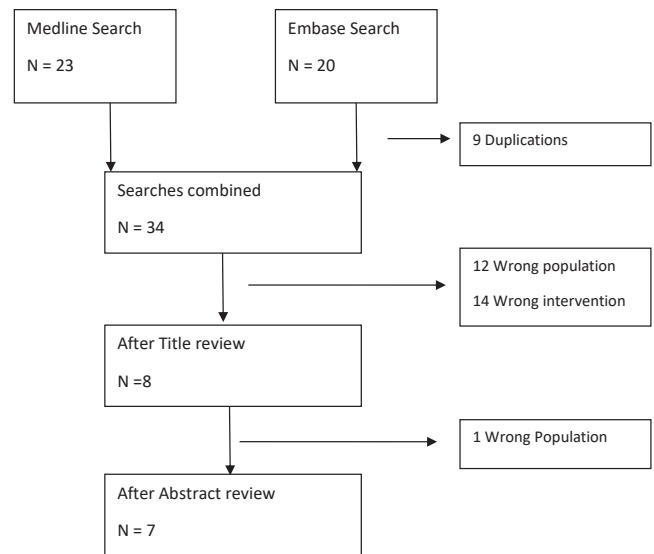


Figure 1. — Flow diagram of Review Process.

supination of 90 degrees²⁴. Gao et al.²⁴ reported the management of partial articular radial head fractures and reported mean flexion arc 139 degrees, pronation 86.5 degrees, and supination 87.4 degrees. The final three studies reported rates of a normal range of motion that ranged from 67% to 86%, with the commonest loss of motion being 10 to 30 degrees of extension^{20,21,22}.

COMPLICATIONS

The complication rate was reported in all studies and varied from 0 to 43%. The pooled complication rate for all studies was 24%. All studies reported a 100% union rate. The highest complications were elbow stiffness (7%), superficial radial nerve neuropraxia (7%), and malunion (5%). Keller et al.²² reported three complications in their six patients with two cases of malunion and one case of avascular necrosis, although this AVN was after a fracture-dislocation of the elbow. Kaziz et al. reported the second-highest complication rate at 43%, with the majority (50%) of these down to joint stiffness²¹. No study reported any patients requiring revision surgery.

DISCUSSION

The main finding from this systematic review is that intramedullary fixation for radial head and neck fractures can provide reasonable and reliable function and range of motion. The reported mean ranges of MEPs (81.8 to 97.9) and Quick DASH score (2.33 to 6.81) suggest at least comparable outcomes from alternative techniques in the literature. Wu et al.²⁷ compared the MEPs using the tripod technique (mean 87.7 (75-100)),

Table II. — Summary of studies reporting use of intramedullary fixation for radial head and neck fractures.

Study	Study Design	Population	Intervention (s)	Mean Follow up	Outcome	Results
Singh et al. 2018 ²⁰ N = 7	Prospective case series	Broberg-Morrey type I and II 5 men, 2 women 3 associated radial head fractures	TENS nail +/- K wire 1 week plaster Passive flexion 1 week and pronation/supination from 3 weeks TENS removed 6 weeks	12 months	Union ROM MEPs Oxford Elbow Score Complications	100% union (mean 6 weeks) 86% normal ROM – 1 patient lost 10 degrees of flexion and pronation MEPs 97.9 (85-100) Oxford elbow score 47.6 (45-48) Complications 14.2%
Kaziz et al. 2018 ²¹ N = 14	Retrospective case series	Mason type I (n=4), Mason type II (n=7) and Mason III (n=3) Mean age 44.2 years (28-67) 8 men, 6 women Mean time to surgery 2.1 days (1-4)	2mm K wire 2 weeks plaster Active assisted ROM from 2 weeks K wire removed after 2 months	86 months (12-120)	Union ROM MEPS VAS pain	100% union (mean 6.9 weeks) ROM 78% normal – 3 restricted 10-30 degrees extension MEPS 95.6 (85-100) VAS pain 0.2 (0-4) QuickDASH 6.4 (7-22) Complications 43% – 3 elbow stiffness – 1 neuropraxia – 1 infected granuloma – 1 malunion with 20 degrees angulation
Keller et al. 1994 ²² N = 6	Retrospective case series	Radial neck fractures with angulation 25-90 degrees Age 16-48 years Time to surgery 24 hours	2 or 3mm K wire or titanium pin Plaster for 2-3 weeks then physio Wire removed after 9 months	Unknown	Union ROM Complications	100% union ROM 67% normal – 2 deficits of less than 20 degrees Complications 50% – 1 AVN (fracture dislocation) – 2 malunion (under 15 degrees)
Bushu et al 2019 ²³ N = 8	Retrospective case series	Mason III (over 30 degrees angulation) Mean age 31.3 years 4 men, 4 women Dominant hand 37.5% FOOSH 6, RTC 2 Acute (mean 4 days (1-7)	Plaster for 2 days then hinged brace 8 weeks Active assisted from 2 weeks Removal implant 8 weeks	9 months	ROM MEPS Complications	ROM – Flexion 0-142.5 degrees – Pronation 96.25 degrees – Supination 90 degrees MEPS 81.8 – Very good 75% – Good 25% Complications 0%
Gao et al. 2019 ²⁴ N = 12	Retrospective case series	Partial articular radial head fractures involving over third of surface and 2mm displaced Mean age 40 years (21-58) FOOSH 6, sport 4, RTC 2 Acute injury (mean 3.2 (2-8)	TENS Sling for 1 week Early mobilisation No sport 3 months	21.8 months (12-28)	ROM QuickDASH VAS Pain MEPs Complications	ROM – Flexion 139 +/-3.13 – Pronation 86.5 +/- 2.75 – Supination 87.41 +/-2.53 QuickDASH 2.33 +/-4.56 VAS pain 0.33 +/-0.78 MEPs 93.75 +/-5.28 (85-100) – Excellent 83% – Good 17% Complication 17% both due to sensory loss of superficial radial nerve

Sandmann et al. 2016 ²⁵ N = 7	Retrospective case series	Mason type III fractures Mean age 39 years (23-90) 5 men, 2 women Acute injuries (mean 2.9 (1-7)	TENS Plaster 2 days then active assisted ROM Sport 3 months	36 months (6-64)	Union VAS pain QuickDASH MEPs Complications	100% union VAS pain 0.6 (0-4) QuickDASH 6.81 +/- 10.42 (0-27) MEPs 95.71 +/- 732 (85-100) – Excellent 71% – Good 29% Complication 14.2% due to superficial radial nerve neuropraxia
Serbest et al. 2015 ²⁶ N = 1	Cases report	Radial neck fracture 52 degrees angulation 37 year old Male	K wire 1.6mm 2 weeks plaster then active ROM Wire out at 4 weeks	Unknown	Union ROM	Union at 3 months ROM – Flexion 145 degrees – Pronation 90 degrees – Supination 90 degrees

TENS – titanium elastic nails, ROM – range of motion, MEPs – Mayo Elbow Performance Score, VAS pain – Visual Analogue Score pain, AVN – Avascular Necrosis, FOOSH – fall on outstretched hand, RTC – road traffic collision.

radial head arthroplasty (85.5 (65-100)), and plate fixation (83.2 (65-85)) and demonstrated no significant difference between the groups (p=0.56). Cristofaro et al.²⁸ assessed the QuickDASH in 80 patients undergoing radial head replacement and reported a mean QuickDASH score of 13. The range of motion reported by Bushu et al.²³ (mean flexion arc 142.5 degrees, pronation 96.25 degrees, and supination of 90 degrees) and Gao et al.²⁴ (mean flexion arc 139 degrees, pronation 86.5 degrees, and supination 87.4 degrees) again appear at least comparable to that reported in the literature for other techniques. Wu et al.²⁷ compared the three main alternative techniques; tripod fixation (mean flexion arc 133 degrees, pronation 75 degrees, and 78 supination degrees), radial head arthroplasty (mean flexion arc 116 degrees, pronation 70 degrees, and supination 72 degrees) and radial plate fixation (mean flexion arc 115 degrees, pronation 57.5 degrees and supination 59 degrees). Any potential improved ROM and function from the intramedullary technique may be explained by avoiding local soft tissue damage and reducing subsequent risk of peri-implant scarring and complications¹¹⁻¹⁴.

The complication rate in the current systematic review was relatively high at 24% (range 0-50%). However, no patients required a repeat procedure or revision surgery other than to remove the intramedullary device as planned. One complication specific to the intramedullary technique was superficial radial nerve irritation or neuropraxia that occurred in 7% of cases. Additional concerns over this technique could relate to a loss of reduction, but this occurred in only three cases (5%), and even in these cases, malunion resulted in under 20 degrees of angulation. Potential benefits of the intramedullary technique are the avoidance of soft tissue stripping at the fracture site with a theoretical reduced risk of AVN and heterotopic ossification; this appeared to be the case with a 100% union rate across the studies, only 1 case of AVN was reported (1.8%) when the technique was employed for a fracture dislocation and no cases of heterotopic ossification.

The complication rates associated with the alternative surgical techniques are comparable in the literature, but the reported revision rates for these other techniques are higher. However, most previous literature on these alternative techniques includes patients with both simple radial head/neck fractures and complex elbow injuries where intramedullary fixation is not indicated. Pike et al.²⁹ reported results after open reduction and internal fixation of isolated radial head fractures. They demonstrated major complications in 13% and 3% rate of significant stiffness requiring secondary capsular

release. Watters et al. reported on patients undergoing either plate fixation or radial head arthroplasty as treatment for terrible triad injuries and demonstrated a revision rate of 28%³⁰. Cristofaro et al.²⁸ reported the management of acute unreconstructable fractures of the radial head with radial head replacement (n=119 patients). They reported a 25% reoperation rate, of which 70% occurred within 1 year after implantation. Wu et al.²⁷ compared complications rates for multiple techniques and reported the highest after plate fixation, followed by screw fixation and arthroplasty (50% vs. 18.8% vs. 15.4%, p=0.048). In addition, the authors reported 33% of patients undergoing radial head plating required revision surgery and 6.25% after tripod fixation²⁷. This apparent reduction in revision rate after the intramedullary fixation technique may be explained partly by avoiding any local trauma or soft tissue damage at the time of surgery¹¹⁻¹⁴. However, the subgroup of the radial head and neck fractures managed by intramedullary fixation may have been less significant injuries and associated with a lower number of concomitant injuries.

Limitations of this systematic review include that the studies only provide level IV and V evidence and provide only 55 patients in total for analysis. Heterogeneity in fracture types, surgical techniques, and post-operative care limit collation of data. Lack of any control groups means that direct comparison to other surgical techniques is not possible. Table I illustrates the MINORS criteria, which ranged from 10 to 14, showing the overall quality of the papers included was moderate to low.

However, this review has given an overview of this relatively unused technique in an adult population and has demonstrated at least comparable function results to alternative surgical techniques. Although complications rates are similar, the risk of AVN and HO appear lower, and the revision rate appears lower than radial head arthroplasty, plate fixation, and tripod fixation. However, the included studies report outcomes in a subset of radial head/neck fractures in a stable elbow. This limits the direct comparison to previous studies, which tend to include these fractures and more complex injuries. Therefore, further robust studies are required to directly compare intramedullary fixation with plate fixation and tripod techniques.

CONCLUSION

Intramedullary fixation for radial head and neck fractures appears to provide an alternative treatment option that produces reliable results in union, ROM,

and functional outcomes for patients with a specific subset of fractures.

REFERENCES

1. Duckworth AD, Clement ND, Jenkins PJ, Aitken SA, Court-Brown CM, McQueen MM (2012). The epidemiology of radial head and neck fractures. *J Hand Surg Am* 37(1):112e9.
2. Conn J, Wade P (1961). Injuries of the elbow: a ten year review. *J Trauma* 1:248-68
3. Wilkins KE (1984). Fractures of the neck and head of the radius. In: Rockwood CA, editor. *Fractures in children*. Philadelphia: J.B. Lippincott Cp. p. 502e21.
4. Schmidt-Horlohe K, Siebenlist S, Stockle U, Pichl J, Hoffmann R (2011). Fractures of the radial head and neck. *Z Orthop Unfall*. 149(6):69-86 (quiz e87-68).
5. Burkhart KJ, Gruszka D, Frohn S et al (2015). Locking plate osteosynthesis of the radial head fractures: clinical and radiological results. *Unfallchirurg*. 118(11):949-56.
6. Zwingmann J, Welzel M, Dovi-Akue D, Schmal H, Südkamp NP, Strohm PC (2013). Clinical results after different operative treatment methods of radial head and neck fractures: a systematic review and meta-analysis of clinical outcome. *Injury* 44:1540-50.
7. Cronlein M, Zyskowski M, Beirer M et al (2017). Using an anatomically preshaped low-profile locking plate system leads to reliable results in comminuted radial head fractures. *Arch Orthop Trauma Surg* 137(6):789-795.
8. Lipman MD, Gause TM, Teran VA, Chhabra AB, Deal DN (2018). Radial head fracture fixation using tripod technique with headless compression screws. *J Hand Surg Am* 43(6):575.
9. Wu PH, Dixit A, Tan DMK, Shen L, Chee YH(2017). Prospective study of surgical fixation of radial head fractures using cannulated headless compression screws for simple and complex radial head fractures. *J Orthop Surg (Hong Kong)* 25(2).
10. Rebgetz PR, Daniele L, Underhill ID, Ochsner A, Taylor FJ (2019). A biomechanical study of headless compression screws versus a locking plate in radial head fracture fixation. *J Shoulder Elbow Surg* 28(4):e111-e116.
11. Ries C, Muller M, Wegmann K, Pfau DB, Muller LP, Burkhart KJ (2015). Is an extension of the safe zone possible without jeopardizing the proximal radioulnar joint when performing a radial head plate osteosynthesis? *J Shoulder Elbow Surg* 24(10):1627-34.
12. Kang HJ, Shin SJ, Kang SS (2012). Nonunion of the radial neck following operative treatment for displaced radial head and neck fractures. *Acta Orthop Belg* 78(5):597-602.
13. Li SL, Lu Y, Wang MY (2015). Is cross-screw fixation superior to plate for radial neck fractures? *Bone Joint J* 97-B:830-5.
14. Young S, Letts M, Jarvis J (2000). A vascular necrosis of the radial head in children. *J Pediatr Orthop* 20:15-8.
15. Narang AM, Pandey AA, Bhat M (2020). Management of Severely Displaced Radial Neck Fractures in Children: A Systematic Review and Meta-analysis of Outcomes. *Indian Journal of Orthopaedics* 54(1):60-68
16. Shabtai I, Arkader A (2016). Percutaneous Reduction of Displaced Radial Neck Fractures Achieves Better Results Compared With Fractures Treated by Open Reduction. *J Pediatr Orthop* 36 Suppl 1:S63-6.
17. Serbest S, Gürger M, Tosun HB, Karakurt L (2015). Closed reduction and intramedullary pinning in the treatment of adult radial neck fractures: a case report. *Pan Afr Med J* 20:434.

18. Moher D, Liberati A, Tetzlaff J, et al (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6:e1000097.
19. Slim K, Nini E, Forestier D, et al (2003) Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg* 73:712-716.
20. Singh N, Pandey CR, John R, Singh R, Tamang B, Bhandari S (2018). The effectiveness of a modified Metaizeau technique in fixation of adult radial neck fractures: a prospective study with a modification of the Broberg-Morrey classification. *J Shoulder Elbow Surg* 27:411-417.
21. Kaziz H, Benzarti S, Triki MA, Mouelhi T, Naouar N, Ayeche ML (2018). Outcome of intramedullary pinning of isolated radial neck fractures in adulthood. *J Shoulder Elbow Surg* 27:1650-1655.
22. Keller HW, Rehm KE, Helling J (1994). Intramedullary reduction and stabilisation of adult radial neck fractures. *J Bone Joint Surg Br* 76(3):406-408.
23. Bushu H, Singh SR, Singh LJ, Siddharth S (2019). Radial neck fracture fixation by Metaizeau technique in adults. A case series and review of literature. *J Orthop Trauma Rehab* 26(1):18-22.
24. Gao X, Yin HL, Zhou GJ (2019). Minimally invasive treatment of mason type II radial head fracture by intramedullary pinning. *Orthop Surg* 11:879-885.
25. Sandmann GH, Cronlein M, Neumaier M et al (2016). Reduction and stabilisation of radial neck fractures by intramedullary pinning: a technique not only for children. *Eur J Med Res* 21:15.
26. Serbest S, Gurger M, Tosun HB, Karakurt L (2015). Closed reduction and intramedullary pinning in the treatment of adult radial neck fractures: a case report. *Pan African Medical Journal* 20:434.
27. Wu H, Shen L, Chee YH (2016). Screw fixation versus arthroplasty versus plate fixation for 3-part radial head fractures, *Journal of Orthopaedic Surgery* 24(1):57-61
28. Cristofaro CD, Carter TH, Wickramasinghe NR, McQueen MM, White TO, Duckworth AD (2019). High Risk of Further Surgery After Radial Head Replacement for Unstable Fractures: Longer-term Outcomes at a Minimum Follow-up of 8 Years. *Clin Orthop Relat Res* 477(11):2531-2540.
29. Pike JM, Grewal R, Athwal GS, Faber KJ, King GJW (2014). Open reduction and internal fixation of radial head fractures: do outcomes differ between simple and complex injuries? *Clin Orthop Relat Res* 472(7):2120-2127.
30. Watters TS, Garrigues GE, Ring D, Ruch DS (2014). Fixation versus replacement of radial head in terrible triad: is there a difference in elbow stability and prognosis? *Clin Orthop Relat Res* 472(7):2128-35.