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ΜΕΤΑΠΤΥΧΙΑΚΗ ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

Meta-analysis of ultrasound-guided versus conventional vascular access in cardiac electrophysiology procedures

Μετα-ανάλυση της καθοδηγούμενης με υπέρηχο έναντι συμβατικής αγγειακής προσπέλασης σε καρδιακές ηλεκτροφυσιολογικές επεμβάσεις

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Abstract

Introduction: Electrophysiology (EP) procedures are nowadays the gold-standard method for tachyarrhythmia treatment with impressive success rates, but also with a considerable risk of complications, mainly vascular. Ultrasound (US)-guidance for vascular access has shown promising results in decreasing the risk of vascular complications in various interventional fields, including EP.

Purpose: To evaluate the safety of US-guided femoral vein access in cardiac EP procedures compared to the traditional anatomic landmark-guided method.

Methods: We searched Pubmed, Embase, Web of Science and Cochrane electronic databases for relevant entries, dated from January 1st 2000 to June 30th 2021. Only observational studies and randomized controlled trials were included in the analysis. Data extraction included study details, patient characteristics, procedure details and all types of vascular complications.

Results: 9 studies (1 randomized controlled trial and 8 observational), with 7,858 participants, were included in the meta-analysis. Overall vascular complication rates were significantly decreased in the US-guided group compared to the control group (1.2 versus 3.2%, RR = 0.38, 95% CI, 0.27-0.53), in all EP procedures. The event reduction effect was significant for both major and minor vascular complications.

Conclusion: US-guided vascular access in EP procedures is associated with significantly reduced vascular complications, compared to the standard anatomic landmark-guided approach.

Keywords: ultrasound, vascular access, catheter ablation, electrophysiology, complications

Περίληψη

Εισαγωγή: Οι ηλεκτροφυσιολογικές (ΗΦ) επεμβάσεις αποτελούν σήμερα τη μέθοδο εκλογής για τη θεραπεία ταχυαρρυθμιών με εντυπωσιακά ποσοστά επιτυχίας, αλλά και με σημαντικό

κίνδυνο επιπλοκών, κυρίως αγγειακών. Η υπερηχογραφικά καθοδηγούμενη αγγειακή προσπέλαση έχει δείξει υποσχόμενα αποτελέσματα στην ελάττωση του κινδύνου επιπλοκών σε διάφορα επεμβατικά πεδία, συμπεριλαμβανομένης και της ηλεκτροφυσιολογίας.

Στόχος: Να εκτιμηθεί η ασφάλεια της καθοδηγούμενης με υπέρηχο μηριαίας αγγειακής πρόσβασης στις ΗΦ επεμβάσεις, συγκριτικά με τη συμβατική, με ανατομικά σημεία καθοδηγούμενη μέθοδο.

Μέθοδοι: Αναζητήσαμε τις ηλεκτρονικές βάσεις δεδομένων Pubmed, Embase, Web of Science και Cochrane για σχετικές καταχωρήσεις, με ημερομηνία από την 1η Ιανουαρίου 2000 έως τις 30 Ιουνίου 2021. Στην ανάλυση συμπεριλήφθηκαν μόνο μελέτες παρατήρησης και τυχαιοποιημένες ελεγχόμενες κλινικές δοκιμές. Η εξαγωγή δεδομένων περιλάμβανε λεπτομέρειες της μελέτης, χαρακτηριστικά ασθενών, στοιχεία της επέμβασης καθώς και όλους τους τύπους αγγειακών επιπλοκών.

Αποτελέσματα: 9 μελέτες (1 τυχαιοποιημένη κλινική δοκιμή και 8 μελέτες παρατήρησης), με 7.858 συμμετέχοντες, συμπεριλήφθηκαν στη μετα-ανάλυση. Τα συνολικά ποσοστά αγγειακών επιπλοκών βρέθηκαν σημαντικά ελαττωμένα στην ομάδα που χρησιμοποιήθηκε υπερηχογραφική καθοδήγηση, σε σύγκριση με την ομάδα ελέγχου (1,2 έναντι 3,2%, RR = 0,38, 95% CI, 0,27 - 0,53), σε όλες τις ΗΦ επεμβάσεις. Η επίδραση μείωσης των αγγειακών επιπολοκών ήταν σημαντική τόσο για μείζονα όσο και για ελάσσονα συμβάντα.

Συμπέρασμα: Η καθοδηγούμενη με υπέρηχο αγγειακή προσπέλαση κατά τη διάρκεια ΗΦ επεμβάσεων συσχετίζεται με σημαντικά ελαττωμένες αγγειακές επιπλοκές, συγκριτικά με τη συμβατική, καθοδηγούμενη με ανατομικά σημεία, μέθοδο.

Λέξεις-κλειδιά: υπέρηχος, αγγειακή προσπέλαση, κατάλυση με καθετήρα, ηλεκτροφυσιολογία, επιπλοκές

Introduction

Electrophysiology (EP) procedures are currently the cornerstone of tachyarrhythmia treatment, with remarkable success rates. It is estimated that almost 300,000 catheter ablations are performed in Europe annually.[1] However, despite the continuous implementation of cutting-edge technologies, these procedures still have a considerable risk of complications. Among them, vascular access-related complications, including hematomas, bleeding, pseudoaneurysms, arteriovenous fistulas, and retroperitoneal hematomas, are the most common and have been associated with increased risk of morbidity, mortality, and health-care costs.

Several studies have shown the feasibility, efficacy and safety of ultrasound (US) guidance for femoral vascular access, compared to the traditional anatomic landmark-guided (ie. symphysis pubis and anterior superior iliac spine, inguinal ligament and femoral artery impulse) approach, in various patient groups. The US-guided method improves first pass and overall success rates, shortens time to successful cannulation and minimizes the risk of vascular complications.[2-4]

This technique has been adopted as standard practice by several medical specialties, such as anesthetists, emergency physicians, critical care professionals, nephrologists, and pediatricians.[5] However, the majority of electrophysiologists still seem to prefer the conventional method. Evidence on US-guided vascular access in EP procedures emerged during the last decade with encouraging results. However, it is not yet considered as a standard of care in such procedures and has not gained universal application, mainly due to cost and training issues.

The objective of this meta-analysis is to review the recently published data and assess whether femoral vein cannulation under US guidance decreases the risk of vascular complications in EP procedures.

Methods

The study was conducted according to PRISMA guidelines. A comprehensive literature search of Pubmed (MEDLINE), Embase, Web of Science, and Cochrane electronic databases was conducted for the identification of relevant entries. We used the keyword string 'ultrasound' and 'femoral' or 'vascular' and 'electrophysiology' or 'electrophysiological' or 'catheter ablation'. Date filter was applied to include publications from January 1st, 2000 to June 30th, 2021. No language restrictions were applied.

We included prospective and retrospective observational studies and randomized controlled trials (RCTs), which compared the vascular complication rates of the US-guided versus the conventional anatomic landmark-guided technique for percutaneous femoral vein access during any EP procedures. Conference abstracts were not eligible. Two independent reviewers screened the titles and abstracts of the identified reports. The full texts of all potentially relevant papers were then assessed for inclusion in the analysis. Discrepancies were resolved by consensus.

Data extraction included publication details (publication year, authors, countries of origin), study design, enrollment period, inclusion/exclusion criteria, sample size, patient characteristics (age, gender, body weight index, use of antiplatelet and anticoagulant agents before the procedure) and procedure details (type of procedure, puncture needle size, periprocedural anticoagulant administration, vascular access time, first pass success rate, inadvertent arterial puncture, total procedure time, types and rates of vascular complications). The total number of vascular complications was the primary outcome. Secondary outcomes were: i. major vascular complications, ii. minor vascular complications, iii. inadvertent arterial punctures, iv. total vascular complications in atrial fibrillation (AF) ablation procedures. Vascular complications were classified as major in case of a clinically overt hematoma, bleeding, arteriovenous fistula, pseudoaneurysm, or retroperitoneal hematoma,

and required intervention (percutaneous thrombin injection, surgical repair, blood transfusion), prolonged hospitalization, or readmission. All other complications were classified as minor.

We used Review Manager Version 5.4 software for statistical analysis. A random-effects model (Mantel-Haenszel method) was selected for the calculation of pooled intervention effects on dichotomous outcomes. Risk ratios (RR) with 95% confidence intervals (CI) were measured and a two-sided p-value <0.05 on the z-test was considered statistically significant. We also estimated the numbers needed to treat (NNT), deriving from total and major event rates. Forest plots for each intervention effect outline the statistical results. Heterogeneity between studies was assessed by visual inspection of the forest plots and calculation of x^2 heterogeneity statistic tests. Heterogeneity was also considered substantial if the p-value was <0.10 in the chi-square test and if the I^2 statistic exceeded 50%. We did not use funnel plots to assess publication bias since less than 10 studies were used for the analysis of each outcome and it would be difficult to detect asymmetry. Sensitivity analysis was not considered due to the homogenous outcomes of the studies.

Results

The outline of the study selection process is depicted in a PRISMA diagram (Figure 1). Initial electronic database screening identified 587 records. Of them, 570 articles were excluded, due to duplication, not relevance, or not meeting the inclusion criteria. We assessed 17 full-text studies for eligibility. Six congress abstracts, 1 single-arm study, and 1 study not meeting the outcome definitions were excluded. Finally, 9 studies (1 RCT and 8 observational) were included in the meta-analysis.[6-14] The basic study characteristics are summarized in Table 1. Five studies included only AF catheter ablation procedures while 4 studies included all EP procedures. The sample size for each study ranged from 36 to 3420 participants and the

summed study population for the analysis was 7,858 patients; 3,743 in the US (intervention) group and 4,115 in the non-US (control) group.

The total number of vascular complications in both groups was reported in 8 studies. US-guided group had a significantly decreased incidence of total vascular complications compared to non US-guided group (1.2 versus 3.2%, RR = 0.38, 95% CI, 0.27 - 0.53, $p<0.00001$, Figure 2). The rate of major vascular complications was also reduced in the US group (0.7% versus 2%, RR = 0.38, 95% CI, 0.25 - 0.59, $p<0.0001$, Figure 3). NNT were estimated to be 50 and 80 for all and major vascular events respectively. Similar findings resulted from the analysis for minor vascular complications (RR = 0.38, 95% CI, 0.22 - 0.59, $p<0.0004$, Figure 4). All tests for heterogeneity were not significant and the studies were homogenous for overall, major and minor vascular complication outcomes.

For the outcome of inadvertent arterial puncture, there was a relative risk reduction by 76% in the US group compared to the non-US group (2.4% versus 17%, Figure 5). I^2 was measured 50% for this outcome, rendering a moderate heterogeneity of the studies. Five studies included only AF ablation procedures, whereas another one provided data for this patient subgroup. When the analysis was restricted to these studies, we estimated a similar RR reduction, again in favor of the US group (0.41, 95% CI, 0.29 - 0.58, $p<0.00001$, Figure 6).

Discussion

To our knowledge, this is the largest meta-analysis published for this subject, including only RCTs and observational studies. We found a significant risk reduction by 62% for vascular complications for the US-guided femoral venipuncture, compared to the conventional, anatomic landmark-guided technique. The estimated NNT indicate that the adoption of routine use of US for venous access in EP procedures could prevent a considerable number of

vascular complications with a potential beneficial impact on morbidity, hospital stay length, and total costs, especially in high volume EP centers.

Our findings keep in line with the results of a previous meta-analysis., which included 4 observational only trials with 4,605 patients and showed 60% and 66% relative risk reduction in major and minor vascular complications respectively.[15] Only one RCT has been conducted in this specific field until today. It enrolled 320 patients who underwent catheter ablation for AF, randomized in a 1:1 fashion. The study was prematurely terminated due to lower-than-expected complication rates, and no difference in major complication rates was found between the two arms.[11]

The rate of vascular complications during catheter ablation procedures in our study population remains within the ranges of previously published reports.[16] Among EP procedures, AF and ventricular tachycardia ablations have a higher incidence of femoral access complications.(10) This occurs mainly due to multiple and large sheath insertions as well as uninterrupted periprocedural anticoagulation, which is currently the routine practice for AF ablation.[17] Our analysis for only AF ablation studies confirms the previous results. The protective role of US guidance remains at the same level for these high-risk patients, showing 59% relative risk reduction for vascular complications. Interestingly, pre-procedural antiplatelet and anticoagulant treatment does not affect the event rates.[6, 7, 10, 12] US-guidance for venipuncture improves first pass success rates and decreases the total number of attempts as well as inadvertent arterial puncture rates. Thus, it can be helpful for populations with increased risk for vascular complications, such as females, obese, elderly patients, and patients with severe atherosclerosis.[18]

Puncture time is significantly decreased when operators use US for vascular access.[9] In the ULTRA-FAST trial, total puncture time was 369 sec (median, IQR 257-584) in the control group compared to 288 sec (mean, IQR 191-370) in the US group ($p<0.001$).[11] Two

other studies also reported a significant reduction in total procedure time.[8, 12] Nevertheless, the reduction in total procedure time could be due to diverse catheter ablation strategies and increased center experience, since all procedures in the US groups were performed later compared to historical non-US groups.

Another favorable outcome of US-guided vein cannulation is the significantly reduced fluoroscopy time during the procedure, which can be explained by less use of X-ray to advance the guidewire into the inferior vena cava.[11, 14]

The anatomic relationship of the femoral vessels varies significantly among patients.[19] Imaging of the inguinal region with computed tomography revealed that, in the anteroposterior plane, femoral artery overlaps the femoral vein in two-thirds of the patients.[20] Real-time 2-dimensional US allows direct visualization of the vessels and contributes to the diagnosis of anatomic variations, which cannot be predicted if no imaging method is used. Inadvertent arterial puncture, even not considered as a vascular complication itself, may potentially predispose to severe clinical adverse events, especially in cases of uninterrupted anticoagulation.

Valsalva maneuver (VM) increases peripheral venous pressure and the diameter of the femoral vein.[21] Futyma et al. assessed the effectiveness of this technique during US-guided femoral venipunctures in EP procedures.[13] No significant differences in the rates of minor or major adverse events between the VM-supported and standard methods were observed, probably due to the low number of events. However, VM seemed to facilitate venous access and a trend towards a lower incidence of vascular complications was noted. It was suggested that VM can be also performed with the traditional anatomic landmark-guided technique. Moreover, it could be beneficial especially in patients who have anatomical abnormalities or small femoral vein diameters, such as women and underweight individuals.

Puncture needle size was reported in only 3 of the studies included, in which a 18-G (gauge) needle was used. However, there is evidence to support that introduction of a micropuncture needle (21-G) in combination with US guidance could potentially further reduce vascular access complications, especially in the high-risk anticoagulated patients.[22-24]

Generally, physicians do not perform venipuncture under US guidance. Lack of equipment, time consumption, and insufficient training are the most frequently reported limiting factors.[25] However, US-guided femoral puncture in EP procedures has a steep learning curve and does not interfere with the normal workflow.[26] It is estimated that only six to seven cases are needed for operators to reach the beginning of puncture time plateau. Moreover, no difference in puncture times was found between senior operators and fellows.[7] No study about the financial evaluation of the technique has ever been performed. However, an economic analysis estimated an additional cost of less than £10 per procedure. It was also concluded that the implementation of US devices is in the long term cost-effective due to reduced complications.[27]

Real-time US-guided venipuncture is currently recommended for patients undergoing AF ablation and/or electrophysiological procedures by international EP societies as a safer, faster, and more effective technique.[17] However, this method has not yet been widely adopted by electrophysiologists and only a minority uses vascular US devices in the EP lab routinely. We believe that this meta-analysis offers robust data which can influence the current clinical practice.

Limitations

Firstly, only one randomized study was included in the analysis. The majority of data was extracted from observational studies, which forms a potential source of bias. However, the lack of heterogeneity between studies and the high level of significance indicate unbiased results. Secondly, the definitions used for the classification and severity of vascular

complications were not universal and minor discrepancies between studies may exist. Thirdly, subgroup analyses based on patient and procedure characteristics were not performed, since patient-level data were not available. Fourthly, an estimation of publication bias was not feasible due to the small number of studies.

Conclusions

US-guided vascular access in EP procedures is associated with significantly reduced vascular complications, compared to the standard anatomic landmark-guided approach. Based on these findings, routine use of US-guidance for femoral vein cannulation should be considered and US devices may become part of the standard EP lab equipment.

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Tables and figures

Table 1. Basic characteristics of studies included in the analysis

1st author	Year	Country	Design	Enrollment period	EP Procedure	Redo (%)	Sample size (US / non-US)	Age (mean ± SD)	Male (%)	BMI (mean ± SD)	Periprocedural anticoagulation status
Tanaka-Esposito	2013	USA	Single-center, retrospective observational	January 2005-December 2006 (non-US) July 2008-May 2010 (US)	AF ablation	NR	3420 (1511 / 1909)	NR	77.6	NR	UI/I
Errahmouni	2014	Monaco	Single center, retrospective observational	April 2012-October 2012 (non-US) November 2012-June 2013 (US)	All EP procedures	NR	300 (150 / 150)	64.6 ± 17	65.3	28.2 ± 4.5	UI
Wynn	2014	UK	Single-center, prospective observational	May 2012-September 2012 (non-US) October 2012-February 2013 (US)	AF ablation	32	309 (163 / 146)	58.9 ± 10.2	72.5	29.6 ± 4.6	UI
Rodriguez-Munoz	2015	Spain	Single center, prospective observational	NR	All EP procedures	NR	36 (24 / 12)	63.9 ± 19.4	69.4	26.0 ± 4.6	NR
Sharma	2016	USA	Single center, prospective observational	October 2014-May 2015 (non-US) June 2015-January 2016 (US)	All EP procedures	NR	720 (360 / 360)	57.9 ± 16	53.0	30.0 ± 7.0	UI
Yamagata	2017	Czech Republic Japan	Multicenter (4 centers), randomized controlled trial	March 2016-November 2016	AF ablation	37	319 (159 / 160)	63.0 ± 8	61.4	29.6 ± 5.2	UI
Ströker	2018	Belgium	Multicenter (2 centers), observational	June 2012-August 2016 (non-US) August 2016-June 2017 (US)	AF ablation	0	1435 (300 / 1135)	60.0 ± 12.0	65.1	27.0 ± 4.0	UI
Futyma	2020	Poland	Single center, observational	November 2016-April 2019 (US) November 2016-September 2018 (non-US)	All EP procedures	NR	981 (876 / 105)	55.5 ± 16.5	45.2	28 ± 5.5	NR
La Greca	2020	Italy	Single-center, retrospective observational	January 2010-March 2016 (non-US) March 2016-January 2020 (US)	AF ablation (± CTI ablation)	20	374 (224 / 150)	60 ± 6	74	27 ± 3	UI

EP, electrophysiology; US, ultrasound group; non-US, non ultrasound group; BMI, body mass index; AF, atrial fibrillation; NR, not reported; UI, uninterrupted; I, interrupted; CTI, cavotricuspid isthmus

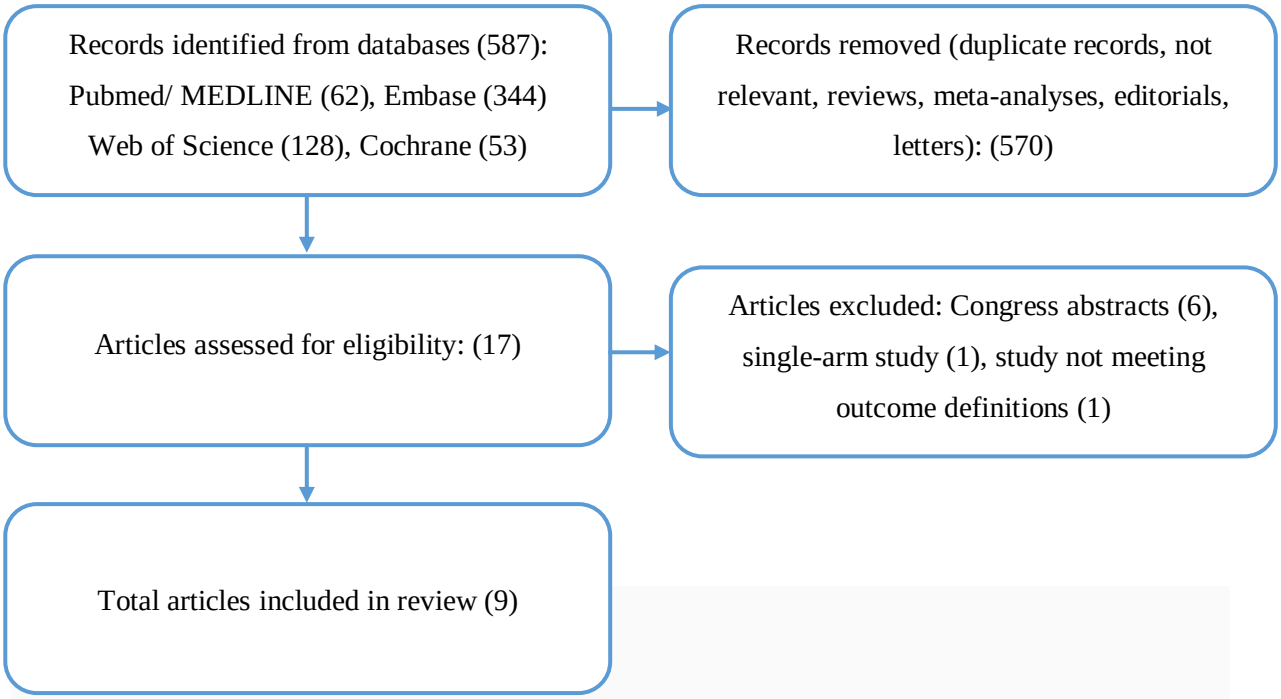

Figure 1: Study flow diagram.

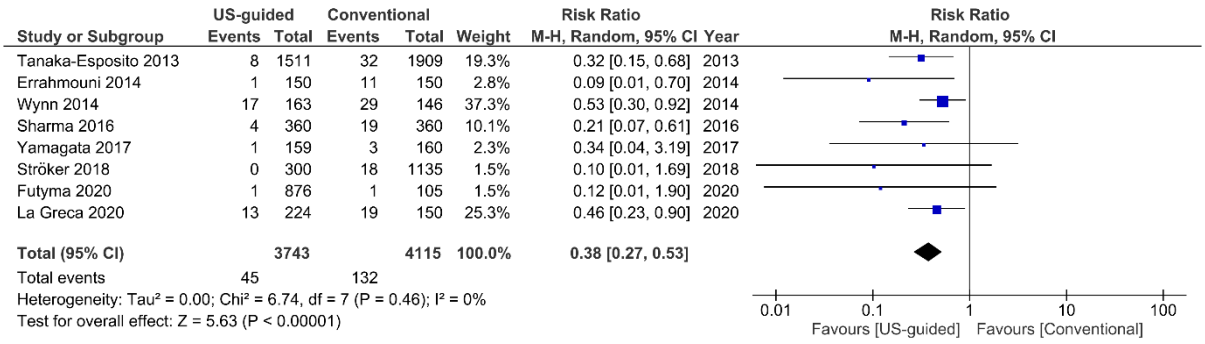

Figure 2: Forest plot of comparison: US-guided vs. Conventional, outcome: Total vascular complications.

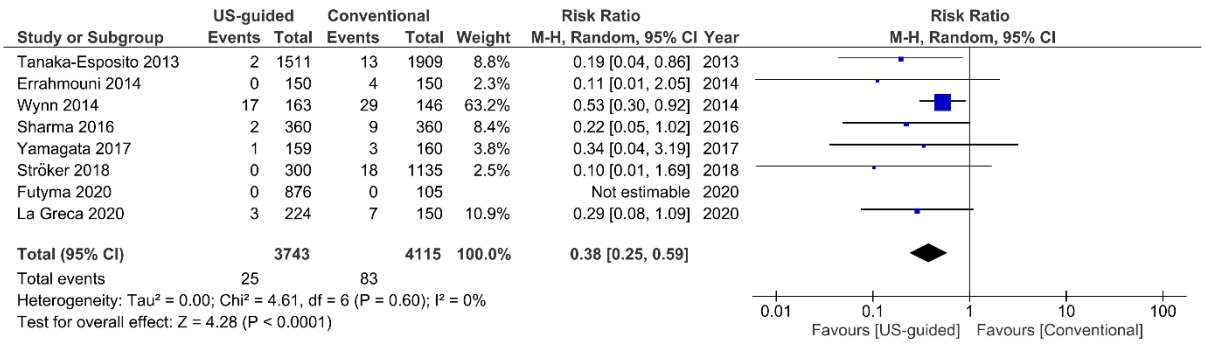

Figure 3: Forest plot of comparison: US-guided vs. Conventional, outcome: Major vascular complications.

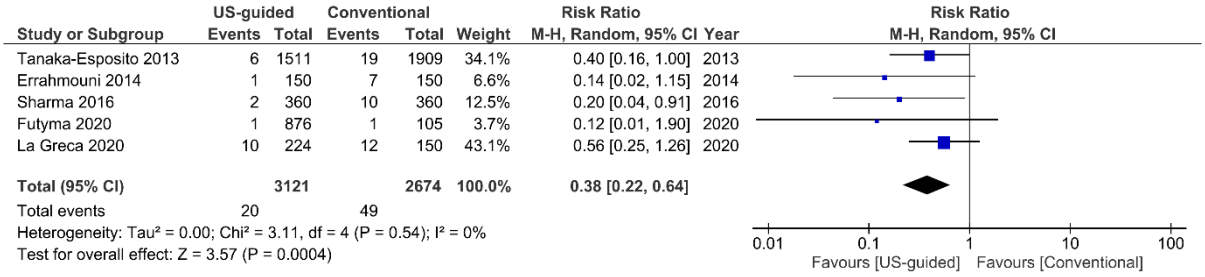

Figure 4: Forest plot of comparison: US-guided vs. Conventional, outcome: Minor vascular complications.

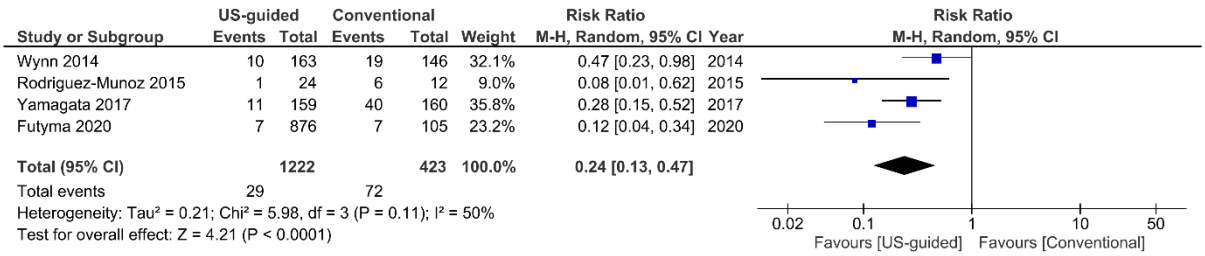

Figure 5: Forest plot of comparison: US-guided vs. Conventional, outcome: Inadvertent arterial puncture.

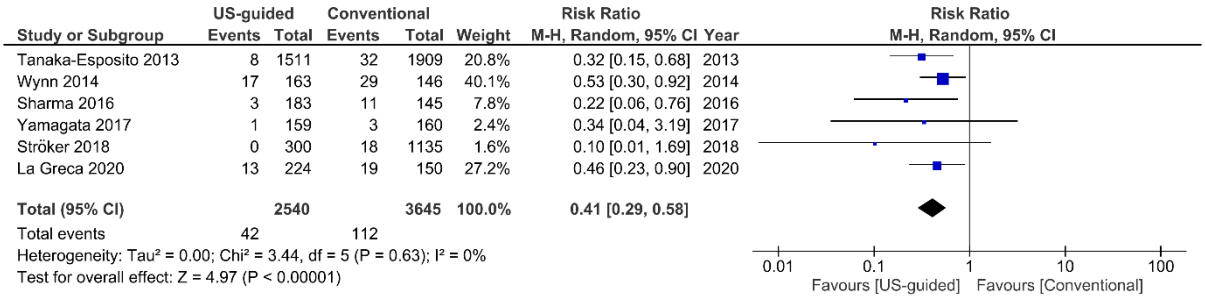

Figure 6: Forest plot of comparison: US-guided vs. Conventional, outcome: Total vascular complications in AF studies.