REVIEW

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# Comparison of Clinical Outcomes of Thyroid Artery Embolization in the Treatment of Thyroid Nodules: A Meta-Analysis

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## Abstract

**Objective:** To compare the clinical outcomes of thyroid artery embolization (TAE) in the treatment of thyroid nodules. **Methods:** A systematic review and meta-analysis were conducted following PRISMA guidelines. Relevant studies published between 1973 and 2023 were identified through PubMed, Cochrane Central, Web of Science, and Google Scholar. Eligible studies included randomized controlled trials and observational studies that evaluated TAE in patients with thyroid nodules. Data were extracted on hormonal levels (FT4, TSH), nodule volume, complications, quality of life, and surgical outcomes. Statistical analyses were performed using Review Manager 5.4.1 with fixed or random-effect models, and results were expressed with pooled mean differences or odds ratios with 95% confidence intervals (CIs). **Results:** Ten studies with a total of 347 patients were included. TAE significantly reduced nodule volume (mean difference: –51.95 mL, 95% CI: –78.58 to –25.33, p = 0.0001), increased TSH levels (mean difference: –0.63 µIU/mL, 95% CI: –1.10 to –0.16, p = 0.009), and reduced surgical blood loss and operative time. The odds ratio for minor versus major complications was 42.60 (95% CI: 17.51 to 103.64, p < 0.00001), indicating a favorable safety profile. Quality of life showed a trend toward improvement, although not statistically significant (OR: 27.72, 95% CI: 0.47 to 1648.47, p = 0.11). **Conclusion:** TAE appears to be a safe and potentially effective procedure for reducing thyroid nodule volume and improving surgical outcomes. However, conclusions should be interpreted cautiously due to high heterogeneity and the observational nature of the included studies.

**Keywords:** Thyroid Artery Embolization- Thyroid Nodule- Hyperthyroidism- Interventional Radiology

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## Introduction

Thyroid gland disorders are prevalent clinical issues, affecting around 9% of women and 2% of men with various thyroid abnormalities. While effective treatments exist for thyroid diseases, some cases necessitate personalized treatment approaches. Traditional therapeutic strategies for hyperthyroidism include antithyroid medications, radioactive iodine therapy, and surgical interventions. However, oral medications can cause severe allergic reactions, thrombocytopenia, liver damage, and other adverse effects. During pregnancy, antithyroid drugs may lead to congenital abnormalities and fetal hypothyroidism. The effectiveness of radioactive iodine therapy can be compromised by amiodarone usage and rapid iodine metabolism. Although surgical procedures can be effective, they are associated with postoperative complications such as hypoparathyroidism, recurrent laryngeal nerve damage, and postoperative bleeding [1]. These challenges underscore the necessity of exploring safer, more effective thyroid treatment alternatives with minimal side effects.

Vascular embolization, used in tumors of the head, neck, and central nervous system, has developed as a definitive or pre-surgical option aiding tumor resection [2]. Interventional radiologists widely use arterial embolization to address vascular disorders and, in oncology, as an adjunct for bleeding control, pain reduction, or as a component of neoplasm management combined with localized chemotherapy. The effectiveness of thyroid artery embolization (TAE) was initially evaluated by Galkin et al., showing reductions in thyroid volume and prevention of nodular goiter recurrence. Current data supports its efficacy in patients with toxic goiter, recurrent goiter, Graves' disease (GD), and thyroid carcinoma [1, 3]. Since Albert von Haller's 1749 description of endothoracic goiter anatomy, cervicomediastinal goiter surgery has been a "challenging" facet of thyroid surgery due to high

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intraoperative risks and postoperative complications, especially severe bleeding [4].

Thyroid artery embolization has been reported in a limited number of cases, primarily indicated for diffuse toxic goiter (Graves' disease). The procedure has shown success in over two-thirds of patients with Graves' disease, significantly reducing thyroid gland volume [5]. Notwithstanding its promising outcomes, there remains a dearth of publications on TAE as a treatment option for thyroid nodules [2]. Hence, this study aims to compare clinical outcomes of thyroid artery embolization in treating thyroid nodules through a meta-analysis of multiple studies, providing more robust evidence-based conclusions.

## Materials and Methods

Literature search strategy: A comprehensive search was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [6] across PubMed, Google Scholar, Cochrane Central, and Web of Science databases with the last search conducted in November 2023. The search terms used included "Thyroid Artery Embolization," "Thyroid Nodules," "Clinical Outcomes," and "Complications." Studies were included if they involved TAE for thyroid nodules, were randomized clinical trials or observational studies (cohort, case-control, or cross-sectional), were published as full-text articles in English or Indonesian, and were published between 1973 and 2023. Exclusion criteria included case reports or series with fewer than five cases, studies with incomplete or inconsistent variable data, and duplicate or previously published studies.

Study Selection Process: Two reviewers (AA and FNH) independently selected studies based on titles and abstracts. Discrepancies were resolved through discussion, and a third reviewer (P) was involved if needed. Studies lacking accessible full-text or incomplete data were excluded. The process followed the PRISMA flow diagram. Data Collection: Authors' names, publication years, countries, therapy methods, tumor characteristics, hormonal levels, volume sizes, complications, quality of life, and effects on thyroidectomy were collected. Microsoft Excel was used to compile data, with the most recent data from articles presenting data from the same study. Raw data on exposures and outcomes were standardized into a uniform table format.

Data Analysis: Fixed-effect or random-effect models were used to analyze the data. The fixed-effect model assumes variability is solely due to chance, while the random-effect model considers both intra- and inter-study variability. Review Manager Version 5.4.1 was used for meta-analysis. Results were presented in forest plots and funnel plots to illustrate combined effect sizes. Publication bias was assessed using funnel plots and risk-of-bias tools. For randomized controlled trials, the Risk of Bias Tool (ROB) was used, while for observational studies, the Quality Appraisal of Case Series Studies Checklist (QACSS) by the Institute of Health Economics (IHE), Edmonton, Canada, was used. Funnel plots visualized the distribution of articles in the meta-analysis. Asymmetric distributions indicated publication bias concerning the relationship between variables.

## Results

*Study Characteristics*

After identification and screening, ten studies met the inclusion criteria [1, 3, 5, 7–13], with a total sample size of 347 patients (Figure 1). Study designs included 7 case-control studies and 3 retrospective/prospective cohort studies. The primary outcomes measured were changes in hormonal levels (FT4, TSHs), nodule volume, complication rates, quality of life, and surgical outcomes (operation duration, blood loss, and drainage volume) (Table 1 & 2). The risk of bias assessment indicated that most analyzed studies had good methodological quality, meeting the majority of QACSS criteria (Table 3). However, areas for improvement include prospective data collection, reporting random variability estimates, and statistical test outcomes. This evaluation highlights the quality and reliability of findings related to thyroid artery embolization for treating thyroid nodules. Addressing these methodological gaps can enhance the strength and reliability of future research.

*Synthesis Data*

*Hormonal Levels (FT4 and TSHs)*

The forest plot (Figure 2) of 7 studies [1,3,7–9,11,12] shows a slight reduction in FT4 levels from 25.36 pmol/L (before) to 22.57 pmol/L (after), with a pooled mean difference of 4.87 pmol/L (95% CI: -0.36, 10.10). However, the confidence interval crosses zero, indicating no statistically significant reduction (p=0.07). While

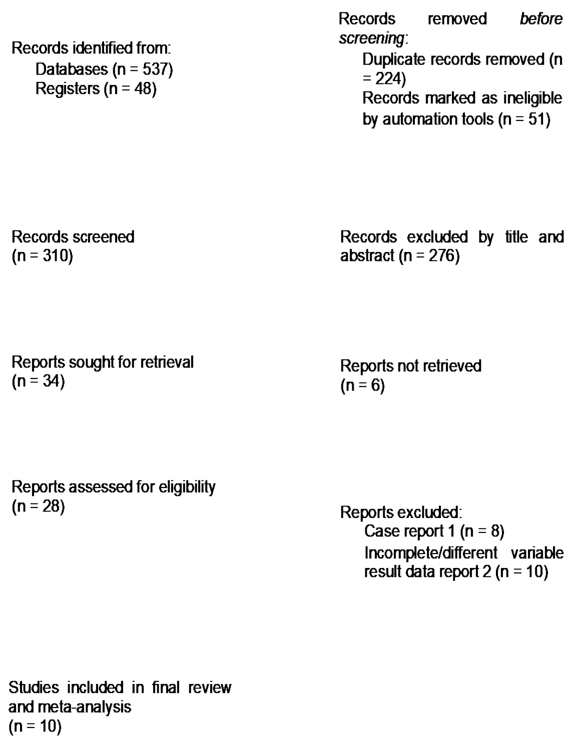


Figure 1. Study Selection Process for the Submitted Systematic Review or Meta-Analysis.

Table 2. Critical Data Appraisal Includes in This Meta-Analysis

| Author & Publication Year | Hormonal level (FT4 (pmol/l) & TSHs (µIU/ml) (Mean ±SD) | | | | Volume (ml) (Mean ±SD) | | Complication (n) | Quality of life (n) | Thyroidectomy w/o SETA (Mean ±SD) | | | Thyroidectomy with SETA (Mean ±SD) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | FT4 BI | FT4 AI | TSHs BI | TSHs AI | BI | AI | | | Time (min) | Blood loss (gr) | drainage (mL) | Time (min) | Blood loss (gr) | drainage (mL) |
| Zhao, W. et al . [7] | 40.87 ± 17.51 | 26.13 ± 9.26 | 0.12± 0.11 | 1.25± 1.06 | - | - | - | - | - | - | - | - | - | - |
| Brzozowski, K. et al [3] | 17,67 ± 4,562 | 7,81 ± 2,25 | - | - | 162 ± 41,83 | 94 ± 27,135 | Minor: 4 | 7 of 12 | - | - | - | - | - | - |
| Tazbir, J. et al. [8] | 17,34 ± 7,755 | 11,9 ± 5,95 | 2,54± 1,136 | 4,28± 2,14 | - | - | - | - | - | - | - | - | - | - |
| Dedecjus, M. et al. [9] | 15,01 ± 3,1 | 20,15 ± 4,55 | 2,96 ± 1,3 | 1,6 ± 1,47 | 90,4 ± 26,4 | 88,9 ± 24,9 | Minor: 16 | 5 of 7 ATC | 123 ± 24 | 138,2± 29.2 | 160 ± 25 | 95,8 ± 26 | 49,9± 12.7 | 92 ± 9 |
| Dedecjus, M. et al. [10] | - | - | - | - | - | - | Minor: 6 | - | 135 ± 25 | 90 ± 26 | 96 ± 36 | 98 ± 35 | 60 ± 12 | 48 ± 25 |
| Kaminski, G. et al. [1] | 17,43 ± 3,716 | 13,29± 2,83 | 0,31± 0,06 | 1,30± 0,27 | 139,3 ± 29,7 | 87,72 ± 18,7 | Minor: 19 | - | - | - | - | - | - | - |
| Zhao, W. et al. [11] | 49,4 ± 13,3 | 42,8± 31,4 | 0,1 ± 0,05 | 0,65± 1,41 | | | Minor: 28, Major: 2 | - | - | - | - | - | - | - |
| Cheng, K. et al. [12] | 16,17 ± 6,60 | 16,06 ± 6,5 | 1,22± 0,49 | 1,82± 0,74 | 84,08± 34,33 | 14,8 ± 6,04 | Minor: 5 | - | - | - | - | - | - | - |
| Yilmaz, S. et al. [5] | - | - | - | - | 122,11± 80,14 | 48,59± 32,43 | Minor: 25, Major: 2 | 50 of 51 | - | - | - | - | - | - |
| Targaglia, F. et al. [13] | - | - | - | - | - | - | Minor: 1 | - | - | - | - | - | - | - |

* Adj: AI, After intervention; BI, Before intervention; SD, Standard Deviation

Table 1. Study Characteristic Include in This Study

| Ref. No | Author & Publication Year | Study Design | Country | Age | Total Case | Clinical Diagnosis | Nodul location | No. of Arteries Embolized | Time Follow-up |
|---|---|---|---|---|---|---|---|---|---|
| [7] | Zhao, W. et al. (2008) | Prospective Cohort Study | China | Mean age 38 (range 25-55) | 41 (final FU 23) | Grave's Disease | Diffuse enlargement | 2-Mar | 3 year |
| [3] | Brzozowski, K. et al. (2012) | Case Series | Poland | Mean age 57 (range 31-83) | 15 (3 Lost-FU) | Grave's Disease & Nodular goiter with compression | Diffuse enlargement | 2-Mar | 4-18 month |
| [8] | Tazbir, J. et al. (2005) | Case Series | Poland | Mean age 65 (range 50-80) | 5 (1 died non TAE-complication) | Inoperable anaplastic thyroid carcinoma | Diffuse involvement | 2-Mar | 1 week |
| [9] | Dedecjus, M. et al. (2007) | Case Series | Poland | Details not provided | 20 | 13 DTC dan 7 ATC | Details not provided | Details not provided | 1-6 day |
| [10] | Dedecjus, M. et al. (2009) | Case Series | Poland | Mean age 60 (range 40-75) | 10 | large toxic goitre | Multinodular goitre | 2-Mar | 12-24 month |
| [1] | Kaminski, G. et al. (2014) | Case Series | Poland | Details not provided | 22 | Retrosternal toxic goiter, Graves diseases | Details not provided | Details not provided | 12 month |
| [11] | Zhao, W. et al. (2007) | Case Series | China | Mean age 32 (range 14-48) | 28 | Grave's Disease | Diffuse enlargement | 2-Mar | 12-22 month |
| [12] | Cheng, K. et al. (2023) | Case Series | Taiwan | Mean age 45 (range 35-55) | 6 | Benign thyroid nodules | Solitary nodule | 1-Feb | 1-3 month |
| [5] | Yilmaz, S. et al. (2021) | Prospective Cohort Study | Turkey | Mean age 55 (range 30-70) | 56 (20 solitary, 36 multinodular/ Volume) --> Lost to follow up 5 | Nodular goiter | Cervical region | 2-Apr | 1-6 month |
| [13] | Targaglia, F. et al. (2019) | Retrospective Cohort Study | Italia | Mean age not provided | 10 | Cervicomediastinal goiter | Various locations | 2-Apr | 6 month |

Table 3. Risk of Bias assessment Using QACSS

| Point of Assessment | Brzozowski, K. et al. [3] | Cheng, K. et al. [12] | Dedecjus, M. et al. [9] | Dedecjus, M. et al. [10] | Kaminski, G. et al. [1] | Targaglia, F. et al. [13] | Tazbir, J. et al. [8] | Yilmaz, S. et al. [5] |
|---|---|---|---|---|---|---|---|---|
| 1. Clearly stated aims and objectives | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 2. Inclusion of consecutive patients | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 3. Prospective data collection | Yes | Yes | No | No | Yes | Yes | No | Yes |
| 4. Clear criteria for inclusion | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 5. Reported demographics | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 6. Reported clinical information | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 7. Reported outcomes and follow-up | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 8. Clear description of the intervention(s) | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 9. Reported adverse events | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| 10. Provided estimates of random variability | Yes | Yes | No | No | Yes | Yes | No | Yes |

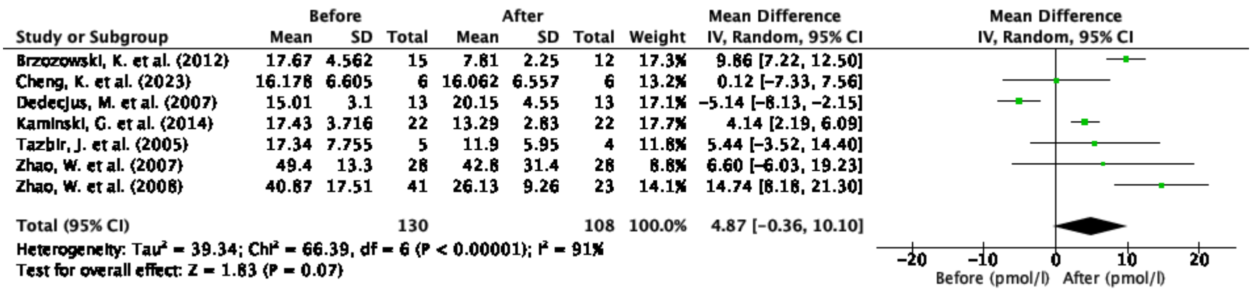


Figure 2. Forest Plot Analysis of Changes in FT4 Hormone Levels

individual studies, such as Brzozowski et al. [3] and Zhao et al. [7], reported significant decreases, high heterogeneity ($I^2$=91%) limits the reliability of the overall results [3, 7]. TSH levels (Figure 3) from 6 studies [1,7–9, 11, 12] before and after intervention, the forest plot shows a significant increase in TSH levels after the intervention, with the cumulative mean rising from 0.78 µIU/ml (before) to 1.68 µIU/ml (after) and a pooled mean difference of -0.63 µIU/ml (95% CI: -1.10, -0.16) (p=0.009). Despite moderate heterogeneity ($I^2$=78%), the results consistently demonstrate the intervention's effectiveness in improving thyroid function.

*Nodule Volume*

The forest plot (Figure 4) of 5 studies [1, 3, 5, 9, 12] demonstrates a significant reduction in thyroid nodule volume following the intervention, with the cumulative mean decreasing from 124.35 ml (before) to 67.66 ml

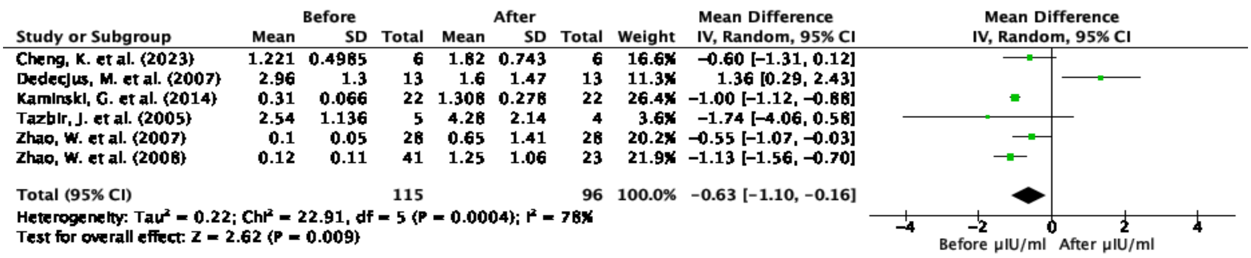


Figure 3. Forest Plot Analysis of Changes in TSHs Hormone Levels

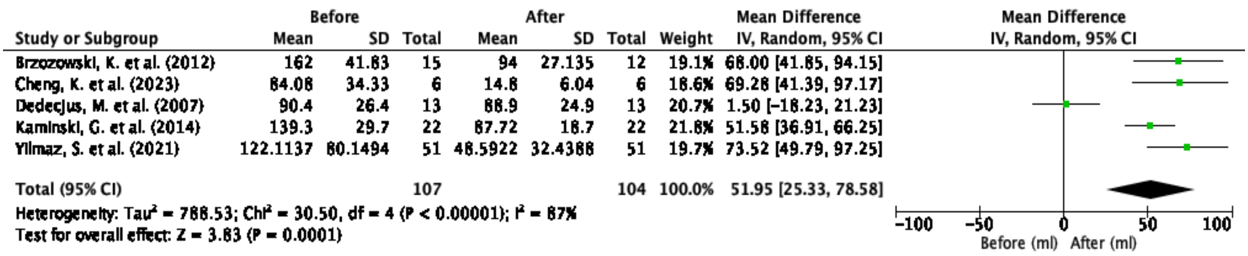


Figure 4. Forest Plot Analysis of Changes in Nodule Volume

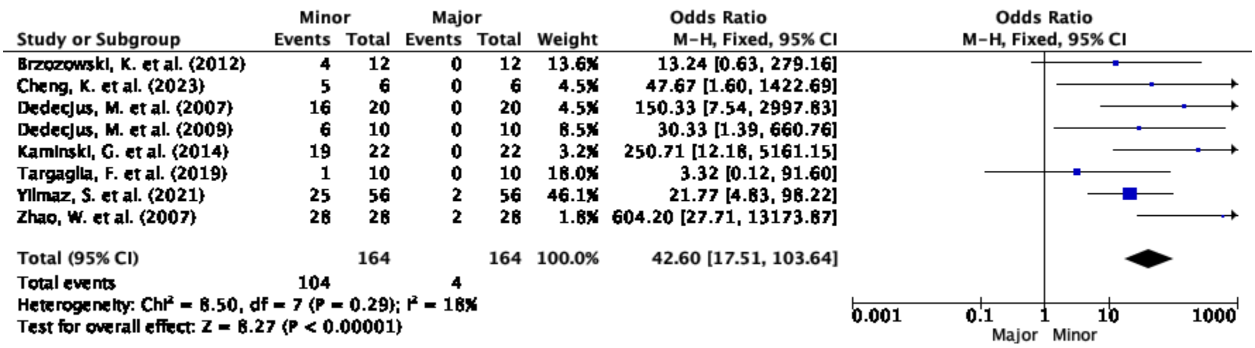


Figure 5. Forest Plot Analysis of Complication Related to TAE

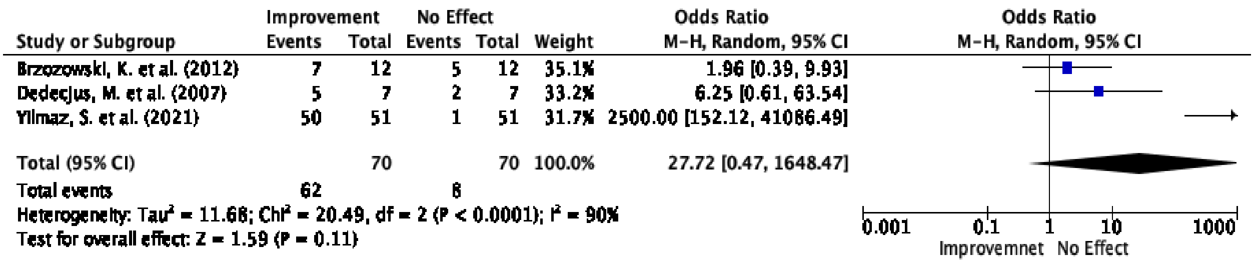


Figure 6. Forest Plot Analysis of Quality-of-Life after TAE

(after), representing an approximate 45.6% reduction in volume. The pooled mean difference is 51.95 ml (95% CI: 25.33, 78.58), indicating a statistically significant reduction (p=0.0001). All studies included in the analysis reported decreases in nodule volume, with the largest reductions observed in Brzozowski et al. [3] and Kaminski et al. [1]. Despite high heterogeneity ($I^2$=87%), likely due to variations in study protocols and populations, the overall findings consistently support the effectiveness of the intervention in significantly reducing thyroid nodule size.

*Complications*

The forest plot (Figure 5) shows 8 studies [1, 3, 5, 9–13], minor complications were significantly more likely than major complications with an odds ratio of 42.60 (95% CI: 17.51, 103.64, P < 0.00001). Low heterogeneity ($I^2$ = 18%) indicates consistency across studies, showing a favorable safety profile with minor complications, including transient neck pain, fever, and asymptomatic hypocalcemia, with major complications being rare. Minor issues reported included neck pain [1, 3, 5, 9–12], fever [1, 9, 10], hematomas [9, 10], and transient hypocalcemia [1, 3, 11]. Rare major complications included hoarseness and vocal cord paralysis [5, 13], groin hematoma, and symptomatic hyperthyroidism requiring hospitalization [5]. Most complications resolved spontaneously or with minimal intervention, highlighting the procedure's overall safety.

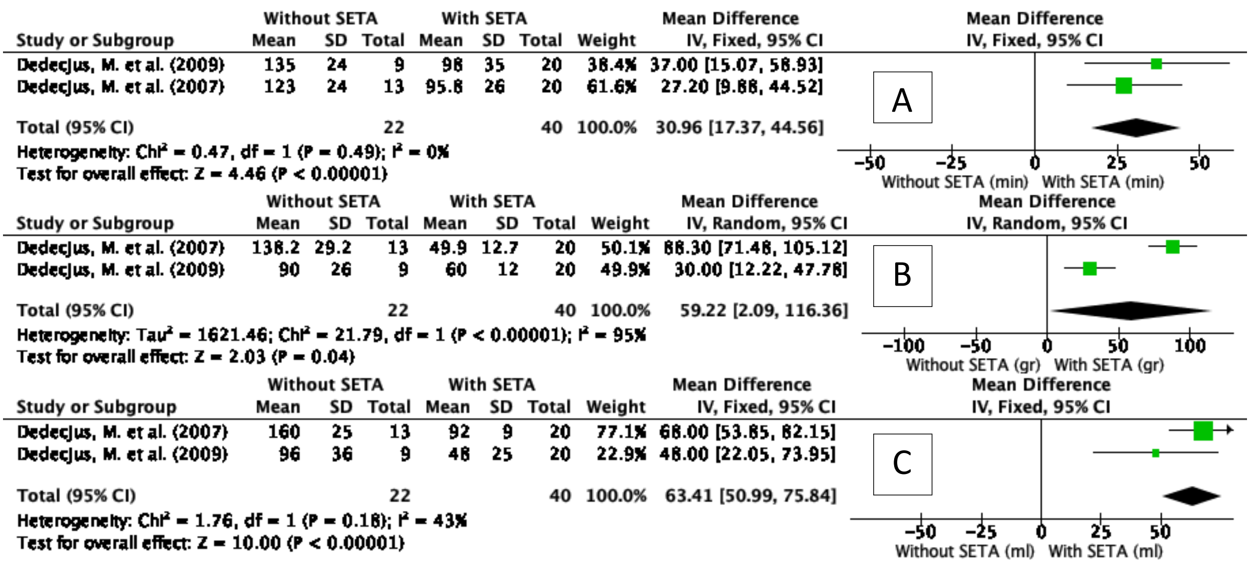


Figure 7. Comparative Analysis of Thyroidectomy Duration (A), bleeding volume (B), and post-operative drain volume (C) with or without TAE

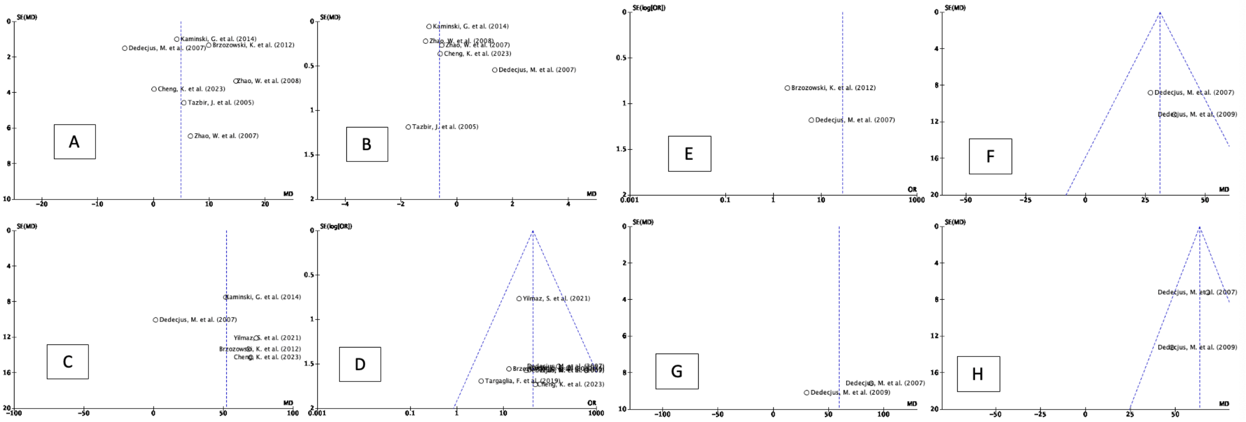


Figure 8. Funnel Plot of FT4 (A), TSHs (B), Volume (C), Complication (D), QOL (E), Surgery duration (F), bleeding volume (G) and post-op drain volume (H) respectively.

*Quality of Life (QOL)*

The forest plot (Figure 6) shows 3 studies [3, 5, 9] an overall odds ratio of 27.72 (95% CI: 0.47, 1648.47) for improvement versus no effect, suggesting a trend favouring improvement with the intervention, though not statistically significant (p= 0.11). High heterogeneity ($I^2$=90%) was observed across the studies, reflecting variability in the results. While Brzozowski et al. [3] and Dedecjus et al. [9] reported positive trends, the wide confidence intervals highlight the need for more consistent evidence.

*Surgical Outcomes*

The forest plot (Figure 7) shows 2 studies [9,10] comparing surgical procedure with or without TAE. Cumulative mean surgery duration was 127.91 minutes without SETA, compared to 97.2 minutes with SETA, resulting in a significant reduction of 30.96 minutes (95% CI: 17.37, 44.56 p-value <0,00001). Both studies showed consistent results, and no heterogeneity was observed ($I^2$ = 0%), highlighting the effectiveness of SETA in reducing surgery time. Cumulative mean blood loss was 121.91 g without SETA, compared to 54.5 g with SETA, resulting in a significant mean difference of 59.22 g (95% CI: 2.09, 116.36, p-value= 0,04). The results demonstrate substantial variability with high heterogeneity ($I^2$ = 95%), but both studies consistently show that SETA reduces intraoperative blood loss, improving surgical outcomes. Without SETA, the cumulative mean drainage volume was 129.09 ml, compared to 61.18 ml with SETA, resulting in a significant reduction of 63.41 ml (95% CI: 50.99, 75.84 p-value <0,00001) and moderate heterogeneity ($I^2$=43%), indicating that SETA effectively reduces postoperative drainage volume, improving recovery outcomes.

The funnel plot (Figure 8) of FT4 (A) shows asymmetry, indicating potential publication bias or variability across studies, with larger studies clustering near the mean and smaller ones more dispersed. The TSH funnel plot (B) appears symmetrical, suggesting consistent results and minimal bias. The volume funnel plot (C) shows significant asymmetry, pointing to heterogeneity or methodological differences. The complication funnel plot (D) is symmetrical, reflecting reliable results with minimal bias in assessing minor versus major complications. The Quality-of-life (QOL) funnel plot (E) shows asymmetry with limited data, suggesting variability influenced by study size. The surgery duration funnel plot (F) is symmetrical, showing consistent results with minimal bias in assessing the intervention's effect on reducing duration. The bleeding volume funnel plot (G) shows asymmetry, suggesting potential bias or variability in outcomes. The drain volume funnel plot (H) is symmetrical, indicating consistent results across studies with minimal bias in assessing drain volume reduction.

## Discussion

Thyroid artery embolization (TAE) has demonstrated significant efficacy in managing hyperthyroidism and large thyroid nodules. Studies included in this meta-analysis [1,12]. consistently reported reductions in FT4 levels, indicating effective control of thyroid hyperfunction. Additional research outside this meta-analysis, such as Ibis et al. [14], confirmed these findings, showing normalization of FT4 levels in patients with Graves' disease following TAE [14]. This reduction is critical, as elevated FT4 levels are associated with severe symptoms, including palpitations, excessive sweating, and weight loss. Furthermore, increased TSH levels post-TAE, reported by Kaminski et al. [1], Cheng et al. [12], and Dedecjus et al. [10], suggest improved thyroid regulation [1,10,12]. Other studies, like Zhao et al. [11], demonstrated similar TSH normalization in cases resistant to conventional therapies .

TAE is also effective in reducing thyroid nodule volume, as documented by Kaminski et al. [1], Cheng et al. [12], and Tartaglia et al. [4]. This reduction is clinically significant as it alleviates compressive symptoms, including difficulty swallowing and breathing. Additionally, TAE facilitates safer surgical interventions by decreasing nodule size, thereby reducing the risk of intraoperative complications. Tartaglia et al. [4] and Ramos et al. [15] highlighted the utility of TAE in reducing hypervascular goiters, minimizing surgical risks, and accelerating patient recovery.

Most complications reported were minor and welltolerated, including transient neck pain, mild fever, and asymptomatic hypocalcemia [1,12]. Rare major complications, such as hoarseness, vocal cord paralysis, and groin hematomas, were noted but resolved with minimal intervention [5, 13]. A case report by Gates et al. [16] demonstrated that TAE can be safely used in emergencies, such as managing superior thyroid artery bleeding after fine-needle aspiration, with no major complications reported during follow-up . These findings emphasize the overall safety of the procedure.

Even though this study statistically shows no significant quality-of-life, some of the studies used it for Graves' disease and another for palliative management. But overall, improvements post-TAE have been widely documented. Studies (e.g., Kaminski et al. [1]; Cheng et al. [12]) reported reduced hyperthyroidism symptoms, enhanced daily functioning, and improved psychological well-being . Additional evidence from Ibis et al. (2007) and Tartaglia et al. [4] highlighted better physical function, reduced compressive symptoms, and enhanced neck aesthetics, further contributing to patients' overall satisfaction [4,14].

As a preoperative procedure, superior thyroid artery embolization (SETA) has proven valuable in reducing surgery duration, intraoperative blood loss, and postoperative drainage volume. Kaminski et al. [1] and Cheng et al. [12] observed significant reductions in surgery duration and blood loss following SETA, while Tartaglia et al. [4] and Dedecjus et al. [10] confirmed decreased postoperative drainage [4, 10]. This reduction is crucial in lowering surgical risks, minimizing complications like infections and hematomas, and expediting recovery.

Study limitations include the small sample sizes, variability in techniques, and inconsistent measurement standards of the analyzed studies, which restrict generalizability and comparability. The majority of included studies were observational and retrospective in nature, which inherently limits the strength of pooled estimates. Additionally, the long time span of included studies (1973–2023) may introduce clinical and methodological heterogeneity due to evolving embolization techniques, imaging modalities, and patient management strategies. Short follow-up durations limit insights into long-term safety, while publication bias and lack of randomization further challenge validity. Addressing these issues requires larger randomized controlled trials (RCTs), standardized protocols, comprehensive complication reporting, and long-term data to better assess the efficacy and safety of TAE. These findings collectively highlight TAE and SETA as effective, safe, and versatile approaches. However, the conclusions must be interpreted with caution due to the limitations of current evidence, particularly the lack of long-term follow-up and randomized controlled trials.

In conclusion, based on these findings, TAE has proven effective in reducing thyroid hormone levels, nodule volume, and complications, as well as improving quality of life and surgical outcomes in patients with various thyroid conditions. Using SETA as a preoperative procedure also provides significant benefits in reducing surgery duration and blood loss. Thus, TAE and SETA can be considered valuable interventions in the clinical management of patients with large and hypervascular thyroid nodules.

Standardized protocols for TAE, including patient selection, techniques, materials, and follow-up, are essential to improve consistency across studies and clinical practice. Larger randomized controlled trials (RCTs) with long-term follow-up are needed to confirm effectiveness, assess delayed complications, and evaluate patient quality of life, including psychological impacts. Combining TAE with other therapies, developing advanced embolization tools, and enhancing healthcare provider training can improve outcomes and reduce risks. Cost-effectiveness studies and detailed complication reporting will support clinical decision-making, while multidisciplinary collaboration between oncology, endocrinology, and interventional radiology ensures comprehensive patient care.

## Author Contribution Statement

Study concept and design: Amirullah Abdi, Prihantono, Faqi Nurdiansyah Hendra. Acquisition of data: Amirullah Abdi, Faqi Nurdiansyah Hendra. Analysis and interpretation of data: Amirullah Abdi, Prihantono, Faqi Nurdiansyah Hendra. Drafting of the manuscript: Amirullah Abdi. Critical revision of the manuscript for important intellectual content: Prihantono, Faqi Nurdiansyah Hendra, Alfian Zainuddin, Nilam Smaradhania, Salman Ardi Syamsu. Statistical analysis: Amirullah Abdi, Faqi Nurdiansyah Hendra, Alfian Zainuddin. Study supervision: Prihantono, Alfian Zainuddin, Nilam Smaradhania, Salman Ardi Syamsu

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*Conflict of Interest*

The authors declare no conflicts of interest related to this study.

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