Aortic remodeling, distal stent-graft induced new entry and endoleak following frozen elephant trunk: A systematic review and meta-analysis

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Abstract

Background: The introduction of the frozen elephant trunk (FET) technique for total arch replacement (TAR) has revolutionized the field of aortovascular surgery. However, although FET yields excellent results, the risk of certain complications requiring secondary intervention remains present, negating its one-step hybrid advantage over conventional techniques. This systematic review and meta-analysis sought to evaluate controversies regarding the incidence of FET-related complications, with a focus on aortic remodeling, distal stent-graft induced new entry (dSINE) and endoleak, in patients with type A aortic dissection (TAAD) and/or thoracic aortic aneurysm. **Materials and methods:** A comprehensive literature search was conducted using multiple electronic databases including EMBASE, Scopus, and PubMed/MEDLINE to identify evidence on TAR with FET in patients with TAAD and/or aneurysm. Studies published up until January 2022 were included, and after applying exclusion criteria, a total of 43 studies were extracted. **Results:** A total of 5068 patients who underwent FET procedure were included. The pooled estimates of dSINE and endoleak were 2% (95% CI 0.01-0.06, I^2 = 78%) and 3% (95% CI 0.01-0.11, I^2 = 89%), respectively. The pooled rate of secondary thoracic endovascular aortic repair (TEVAR) post-FET was 7% (95% CI 0.05-0.12, I^2 = 89%) whilst the pooled rate of false lumen thrombosis at the level of stent-graft was 91% (95% CI 0.75-0.97, I^2 = 92%). After subgroup analysis, heterogeneity for dSINE and endoleak resolved among European patients, where Thoraflex Hybrid and E-Vita stent-grafts were used (both I^2 = 0%). In addition, heterogeneity for secondary TEVAR after FET resolved among Asians receiving Cronus (I^2 = 15.1%) and Frozenix stent -grafts (I^2 = 1%). **Conclusion:** Our results showed that the FET procedure in patients with TAAD and/or aneurysm is associated with excellent results, with a particularly low incidence of dSINE and endoleak as well as highly favorable aortic remodeling. However the type of stent-graft and the study location were sources of heterogeneity, emphasizing the need for multicenter studies directly comparing FET grafts. Finally, Thoraflex Hybrid can be considered the primary FET device choice due to its superior results.

1. Introduction

The management of complex pathologies of the thoracic aorta have always presented a challenge to surgeons due to the high associated risk of morbidity and mortality. The introduction of frozen elephant trunk (FET) technique facilitated total arch replacement (TAR) procedures by shortening the aortic occlusion

time for proximal anastomosis, providing the opportunity of treating complex aorta pathologies in a single-step procedure, or by offering a more optimal landing zone for secondary endovascular intervention if needed [1]. Due to its hybrid approach, FET has gained great popularity in the field of aortovascular surgery, and since its introduction, it has become the mainstay technique for TAR in a wide spectrum of complex thoracic aortic diseases.

The indications for the FET procedure include chronic aortic aneurysms, acute and chronic type B dissections in cases where endovascular treatment is contraindicated, and furthermore, acute or chronic type A aortic dissections (TAAD) [2]. Despite the highly favorable results associated with FET, particularly aortic remodeling in terms of true lumen (TL) flow maintenance and false lumen (FL) obliteration, the rates of reinterventions following the procedure are minor but present [3-6].

Stent graft-induced new entry (SINE) is one of the major complications of FET defined as a new tear occurring either at the distal or proximal end of the stent-graft portion of the FET device that is caused by the stent-graft itself [7]. This complication was first identified and documented by Ninomiya et al. [8] in 2002, but was named "SINE" later on by Dong et al. [7] in 2010. The incidence of distal SINE (dSINE) post-FET has been associated with the stent-graft size and length, aortic pathology type and location, and the distal landing zone of the FET hybrid prosthesis (HP). Other complications of the FET procedure are, but not limited to, endoleak, spinal cord injury (SCI), renal complications, cerebrovascular events and graft kinking. Yet, it is important to note that the incidence of the above postoperative events is lower with FET compared to conventional arch replacement techniques [9, 10, 11].

Several commercial FET HPs exist on the global market, these include Thoraflex Hybrid (Terumo Aortic, Inchinnan, Scotland, UK), E-Vita (JOTEC GmbH, Hechingen, Germany), J Graft Frozenix (Lifeline Co, Ltd, Tokyo, Japan) and Cronus (MicroPort Medical Co, Ltd, Shanghai, China). However, overall evidence in the literature seem to suggest that the Thoraflex Hybrid (or THP) is the superior FET devices on the arch prosthesis market [9, 10]. Nevertheless, the literature also describes controversial evidence on the association between the aforementioned commercially-available FET devices and clinical outcomes. This meta-analysis aimed to provide a wide and comprehensive perspective on the relationship between FET device type and results, including aortic remodeling and other complications such as dSINE and endoleak.

2. Materials and methods

2.1. Search strategy

A comprehensive literature search was conducted using EMBASE, Scopus, and PubMed/MEDLINE databases from inception and up to January 2022, to identify evidence on FET technique used in TAR registering patients with acute or chronic TAADs and/or thoracic aortic aneurysms. To combine all search terms, a Boolean operator was used (**Supplement Table 1**). In addition, to identify additional research papers for the purposes of this review, a manual hand search of references within our retrieved studies was performed. English language and human studies were the only criteria used for results limitation during the literature search.

2.2. Inclusion criteria and data extraction

The present systematic review and meta-analysis was conducted according to the PRISMA guidelines [12]. Results from literature providing complications of hybrid repair of aortic arch only with FET in patients with acute and chronic TAADs and aneurysms were included. Due to the potential doubling of outcomes, review articles were excluded. Also, articles reporting FET outcomes with no clear pathology type or complication, as well as case reports, editorial commentaries and experts' recommendations were excluded. Among studies reported by the same group of researchers, only the latest publication and/or ones with the largest patient populations were considered. Titles and abstracts of all obtained articles were assessed by 2 reviewers independently, and a third reviewers opinion was obtained in cases of discrepancy/uncertainty. Once the abstract was congruent with our inclusion criteria, the full-text article was retrieved and assessed for suitability according to our inclusion/exclusion criteria.

Extracted data from included articles comprised of the first author's name and study publication year, study institution/center name, number of enrolled patients, baseline characteristics (i.e., age, sex, prior medical history and cardiovascular risk factors, and aortic pathologies), operative features related to the FET procedure (i.e., concomitant procedures, duration of procedure, cardiopulmonary bypass time, aortic cross-clamp time, and stent site and type), follow-up outcomes including FET-related complications (i.e., hospital and intensive care unit length of stay, cerebrovascular events, paraplegia, acute kidney injury, in-hospital and 30-day mortality, dSINE and endoleak), FL thrombosis state, and need for re-intervention following FET (i.e., TEVAR).

2.3. Statistical analysis

Data for the outcomes of interest are presented in numbers and percentages and mean values with a 95% confidence interval (CI) were also considered. The measurement of the weighted prevalence of outcomes was performed and is presented in forest plots. Moreover, the conversion of the median for continuous values (e.g., age and length of stay) into the mean was applied as needed. Furthermore, the I^2 statistic was used to quantify the total variability among eligible studies, ascribable to heterogeneity, and reported in percentages with a 95% CI. The I^2 covers the spectrum of 0% indicating no heterogeneity, 25% to 49% as low heterogeneity, 50% to 74% as moderate heterogeneity, and [?]75% as high heterogeneity, according to published guidelines [13, 14]. The random-effects model, where the I^2 value lies above 50%, was utilized, and a fixed-effects model (Mantel – Haenszel method) was used when significant heterogeneity was absent. Regarding the inconsistency among some of the results of observational studies including stent type (Thoraflex Hybrid, E-Vita, Cronus, Frozenix, and mixed/other), location of the study center (Asia, North America, and Europe), and elective/non-elective procedure, subgroup analyses were performed. Publication bias was evaluated by Egger's test and visualized by the funnel plots, and additionally, statistical tests for its asymmetry were employed. The statistical significance was reached by P-values below 0.05. All the statistical analyses were performed using R (version 4.1.2) and STATA (V.16.0) softwares.

2.4. Population characteristics

Forty-three eligible studies were entered into the final analysis, reporting the complications of FET procedure in TAR. The study cohort includes Asian, European, North American, and Brazilian populations.

3. Results

3.1. Baseline characteristics

A total of 79 931 records were collected via online database review, out of which 7345 studies were eligible for abstract screening. After applying the exclusion criteria, 109 records were adopted for full-text screening, and eventually, reported data of 43 studies including 5068 patients who underwent TAR with FET were reviewed [4, 15-56] (**Figure 1**).

Overall, the mean proportion of males out of the patient population included in this meta-analysis was 72.2% (95% CI 70.8-73.6). The most frequently reported risk factor was hypertension (67.6% [95% CI 65.9-69.3]), followed by smoking (19.2% [95% CI 15.6-23.2]). In addition, emergent surgeries accounted for 81.2% (95% CI 78.8-83.5) of individuals (studies in which the urgency of procedures was reported). The pooled means for cardiopulmonary bypass (CPB) time and the aortic cross-clamp time were 220 minutes (95% CI 202.8-237.3) and 136.6 minutes (95% CI 122.8-150.5), respectively. All extracted baseline characteristics and procedural features are summarized in **Table 1** .

3.2. Pooled data synthesis for outcomes of interest

The pooled length of in-hospital stay and intensive care unit stay was found to be 21 days (95% CI 15.9-26, reported by 13 studies including 1227 patients) and 6.2 days (95% CI 4.7-7.7, reported by 15 studies including 1419 patients), respectively. Using the random effects model, the pooled estimates of postoperative dSINE and endoleak were 0.02 (95% CI 0.01-0.06, I^2 = 78%; [**Figure 2**]) and 0.03 (95% CI 0.01-0.11, I^2 = 89%; [**Figure 3**]), respectively. Moreover, the pooled rate of secondary endovascular treatment of aortic

pathologies after FET during follow-up was 0.07 (95% CI 0.05-0.12, I^2 = 89%), depicted in**Figure 4** . Furthermore, the pooled estimates of FL thrombosis at the stent level, the descending thoracic aorta (DTA) level, and the abdominal aorta (AA) level were 0.91 (95% CI 0.75-0.97, I^2 = 92%), 0.61 (95% CI 0.49-0.72, I^2 = 86%), and 0.36 (95% CI 0.25-0.48, I^2 = 88%), respectively (**Supplemental Figures 1A-C**).

Of major postoperative outcomes, the pooled estimate of in-hospital mortality was 0.05 (95% CI 0.04-0.07, I^2 = 52%), which was reported in 20 studies comprising of 2657 patients in total (**Figure 5**). Paraplegia and renal failure were detected in 0.03 (95% CI 0.02-0.04, I^2 = 21%) and 0.11 (95% CI 0.07-0.16, I^2 = 89%) of patients, respectively (**Figures 6 and 7**). In addition, the pooled estimate of cerebrovascular events was 0.06 (95% CI 0.04-0.10, I^2= 89%; **Figure 8**). Lastly, the 30-day mortality rate was 0.06 (95% CI 0.03-0.11; I^2 = 79%; **Figure 9**).

3.3. Subgroup analysis

Subgroup analyses were also conducted based on the type of surgery, FET graft type, and the geographical location of the study center (**Table 2**). The pooled estimates of outcomes in subgroup analyses revealed that the heterogeneity for secondary endovascular treatment during follow-up post-FET period disappeared, as there was no heterogeneity among patients receiving the Cronus (I^2 = 15.1%) or Frozenix (I^2 = 1%) stent-grafts. In addition, amongst patients undergoing emergent surgery, the source of heterogeneity was non-significant (I^2 = 8%). Based on the geographical location of study centers, there was least source of heterogeneity among Asian countries (I^2 = 39.5%). On the other hand, with regards to the development of dSINE, there was no heterogeneity (I^2 = 0%) amongst European studies, including those utilizing Thoraflex Hybrid and E-Vita stent-grafts. Moreover, the pooled estimates of postoperative endoleak were also without heterogeneity (I^2 = 0%) in patients receiving Thoraflex Hybrid as well as those undergoing FET HP implantation in European centers. Other subgroup analyses and their effect on the pooled estimates of outcomes and the heterogeneities are summarized in **Table 2** .

3.4. Publication bias

Based on the Egger's test and the visual inspection of the funnel plots, which revealed asymmetries, the sources of publication bias are almost all the reported postoperative outcomes in our results ($p < 0.050$ for all outcomes) except for in-hospital mortality ($p = 0.254$) and FLT at the level of AA ($p = 0.703$). All Funnel plots are provided as **Supplemental Figures 2A-K** .

4. Discussion

The FET technique has become a consolidated choice for TAR in patients with diffuse aortic pathologies. This is due to its highly favorable results which can be considered superior to conventional arch repair. To elaborate, the FET procedure offers improved aortic remodeling, splendid clinical outcomes, shorter procedure-related times, and a more ideal proximal landing zone for further endovascular completion if necessary [25, 57, 58]. Although providing all those abovementioned benefits, it still comes with a non-negligible risk of negative remodeling, dSINE, and endoleak, which may require secondary intervention, negating its one-step advantage. Yet, the choice of FET device type can greatly influence results [59].

Aortic remodeling, which is well-established in the literature as a valuable prognostic tool for patients undergoing surgical repair of TAAD, is outlined as positive, stable, or negative based on the aortic lumen (AL) and TL diameter changes as well as the extent of false lumen thrombosis (FLT) [58, 60]. According to Dohle et al. [61], and based on the Society of Vascular Surgery standards [62], remodeling is considered positive when there is a [?]10% expansion in TL diameter and/or a reduction in overall AL diameter. Meanwhile, an increase in the size of the FL/AL is classed as negative remodeling. As expected, without significant changes in aortic diameters the remodeling process is regarded as stable [61, 62]. In TAAD, the constant FL antegrade perfusion caused by the intimal entry tears gives rise to aneurysmal deteriorations along the aorta; however, if these entry points remain patent after surgical repair, this presents an important risk factor for aortic dilatation and rupture as well as an increase in the need for further distal reintervention [9, 63]. Additionally, FL expansion has been shown to be associated with the entry's size and location [64].

For example, Turley et al. [65] demonstrated that the presence of major vessels originating from the FL could play a crucial role in the disruption of the FLT process. Occlusion of the FL entries, on the other hand, hampers the antegrade blood flow through the FL which promotes FLT, leading to TL re-expansion and favoring improved distal perfusion [66, 67]. Thus, utilizing longer FET stent grafts aids aortic remodeling through extended coverage of the aorta distally, obliterating any entry tears and stabilizing the diseased intima [9].

Although the exact mechanisms behind the process of aortic remodeling remain unclear, the FET procedure drives excellent aortic remodeling. This is evident in a meta-analysis evaluating 1279 patients with TAAD undergoing TAR with FET where the rate of FLT was found to be 96.8% around the stent graft (or at the DTA level) [68]. Interestingly, the varying extent of remodeling along the aorta (i.e., the stent-graft, DTA, and AA levels) is well-documented in the literature. This was demonstrated by Dohle et al. [69], where after 1 year of follow-up, volumetric calculations found remodeling was 98% at the stent-graft site, 68% from the end of the stent-graft to the coeliac trunk level, and 39% from the coeliac trunk to the aortic bifurcation level. Also, positive (or stable) aortic remodeling rates followed the same descending trend, marking 94%, 64%, and 54% at each respective level. The authors also found a significant increase in the volume of the thrombosed FL after the first year of follow-up, distal to the stent graft. Iafrancesco and his colleagues [58] suggested that the FLT rate influences the AL diameter changes. Here, 99.3% FLT was recorded at the level of mid-DTA compared to 13.9% achieved at the distal AA, confirming our earlier statement on the varying FLT rates along the length of the aorta, with remodeling decreasing more distally [58]. Importantly, our results clearly show an utterly congruent trend as the rate of FLT around the stent graft was 91%, with 61% at the thoracic aorta and 36% at the level of the AA.

As aforementioned, several FET devices are available commercially, the most commonly used being Thoraflex Hybrid, E-Vita, J Graft Frozenix, and Cronus, in this order. However, evidence in the literature supports Thoraflex Hybrid's superiority in clinical outcomes over its competitors. This is no different when it comes to aortic remodeling, as Thoraflex Hybrid has been proven to promote excellent FLT and is associated with significant positive changes in aortic diameters [9, 10, 59]. This is evident in multiple studies, one of which is Mehanna et al. [37] which featured Spearman rank correlation tests to assess the correlation of their results. This testing revealed that aortic remodeling ratios, before and following the procedure, had a moderately positive correlation. The study reported a significant expansion of the TL ratio using Thoraflex Hybrid post-operatively, with a median increase from 0.31 to 0.4 mm ($P = 0.042$), as well as a significant FL ratio decrease from 0.66 to 0.54 mm ($P = 0.02$). The authors also described the unique interrupted pattern of Thoraflex Hybrid stent-graft, which is thought to protect the aortic wall from the substantial forces of blood flow to help achieve excellent aortic remodeling. Overall, it was concluded that the Thoraflex Hybrid is the safest and most efficacious FET device, promoting superior aortic remodeling [37]. Interestingly, a Thoraflex Hybrid study by Usai et al. [70] used volume measurements to assess aortic diameters instead of the computed tomography scanning used in most studies, allowing more accurate measurements to be taken. Similar to Mehanna [37], Usai [70] also found that the Thoraflex Hybrid induced substantial expansion of the TL along with shrinkage and thrombosis of the FL. Prior to the procedure, the mean TL volume was 77.03 cm^3 ($\pm$ 47.96 cm^3); this increased to 133.84 cm^3 at 24 months of follow-up. The long-term analysis of TL volumetric expansion evidenced a statistically significant growth even 2 years after the FET procedure ($P = 0.047$). Another aspect showing Thoraflex Hybrid's superiority over other FET HPs is its outstanding ability to promote aortic remodeling distally, as Usai et al. [70] also noted that the most significant growth in the surface TL measurement was at the level of the diaphragm ($P = 0.00193$). In addition, the results in Fiorentino et al. [51] confirmed that the Thoraflex Hybrid yields TL expansion not only at the level of pulmonary bifurcation (FLT rate = 73.1%) but also at the distal DTA as well as the AA. Furthermore, upon searching the literature, the need for endoprosthetic extensions due to incomplete FLT was found to be less by 6% with the Thoraflex Hybrid in comparison with the E-Vita HP, its main market competitor [71]. To further prove Thoraflex Hybrid's superior efficacy, Shrestha et al. [72] reported a 100% FLT rate among 100 patients in their single-center study. On the other hand, Akbulut et al. [73] observed a 93.9% and 54.5% FLT rate at the pulmonary trunk and diaphragmatic levels, respectively, using the E-Vita graft. Unfortunately,

the use of Frozenix and Cronus FET grafts is geographically confined to only a few countries, thus data on their aortic remodeling performance is limited and would be unreliable for comparisons [9].

Developing SINE is one of the main drawbacks of the FET technique, in which the false lumen patency negatively impacts aortic remodeling by increasing thoracic aorta diameter and thus, increases the need for reintervention [4, 9, 69]. Kreibich et al. reported a significant negative correlation between the TL diameters at the level of the stent graft and the development of dSINE [74]. SINE can develop at any point during follow-up post-FET, and its onset is usually asymptomatic but can progress rapidly [74, 75]. SINE occurs when the stent-graft portion of the FET device induces injury to the intima of the aorta due to the pathological dissection membranes mismatching with the stiffer stent [9]. In addition, evidence in the literature shows that the incidence of dSINE in patients with chronic dissection undergoing FET is higher than in acute patients, which can be attributed to the more advanced fibrotic changes in the chronic dissection membrane [75]. In this regard, Janosi found that AD patients with a longer time interval between diagnosis and intervention were more prone to developing dSINE [75]. Upon searching the literature, the incidence of dSINE following FET was found to be highly variable, ranging from 0-27.3% [50, 74, 76-78]. The abovementioned wide range of incidence described in the literature could be attributed to the differences among stent types, sizes, and the hybrid prosthesis loading process, as well as the patient anatomical/clinical characteristics, and study design. Evidence in the literature suggests that severe graft oversizing as well as using shorter graft lengths are the main contributing causes for dSINE, in addition to adopting a more proximal landing/implantation zone to deploy the stent graft (e.g. zone 2) [9, 10, 59]. Our results showed a pooled estimate of 2% for dSINE after FET with a high heterogeneity which disappeared amongst cases registered by European centers. If left untreated, dSINE can lead to a mortality rate of up to 25%, hence it requires prompt distal reintervention to prevent further FL enlargement or rupture [9, 74]. Importantly, secondary TEVAR intervention can achieve excellent results in this clinical scenario [7, 36]. Moreover, several studies have supported the superiority of TEVAR over open surgical re-intervention, particularly when it comes to mortality and complications [32, 79]. Furthermore, Loschi et al. [41] compared TEVAR reintervention to open surgical reintervention following FET and demonstrated a significantly higher clinical success rate at five years (95% vs 68%, P = 0.022) as well as significantly fewer complications (5% vs 42.9%, P = 0.004) amongst the TEVAR reintervention group. Despite the excellent clinical success for secondary TEVAR after FET, it should only be utilized with caution in patients with connective tissue disorders owing to disputable results reported in the literature [32].

Thoraflex Hybrid's superiority extends to dSINE by demonstrating outstandingly low incidence compared to the other devices. Upon searching the literature, the incidence of dSINE reported in the studies identified ranged from 0-14.5% with Thoraflex Hybrid, 1-18.2% with E-Vita, and 0-27.3% with Frozenix [9,10, 59]. Charchyan et al. [80] compared dSINE incidence with ring-shaped nitinol stent-graft (Thoraflex Hybrid) against Z-shaped nitinol stent-grafts (E-Vita) and distal dissection-specific stent-grafts (Valiant retrograde stent-graft, Medtronic Vascular, Santa Rosa, CA, USA). The results prove that dSINE occurrence is significantly lower with Thoraflex Hybrid than with E-Vita (4.5% vs. 13%, P = 0.043). Another study directly comparing both these grafts is Berger et al. [77], which concluded that Thoraflex Hybrid yields more favorable results. Here, 14.5% of patients in the Thoraflex Hybrid developed dSINE post-FET relative to 18.2% with E-Vita Open (P = 0.19). The Frozenix HP, however, was found to be associated with the highest incidence of dSINE whilst, on the other hand, no dSINE data was identified for Cronus due to its geographical confinement leading to a paucity of data [9, 81]. Lastly, Thoraflex Hybrid's unique circular design and special material have been shown to reduce the stress on the aortic wall, contributing to the excellent dSINE results seen across the literature and in our study [9, 10, 82].

Endoleak after FET has been described across the literature as an unsatisfactory seal at the stent-graft anastomosis site either at its proximal or distal end which usually necessitates secondary intervention. In a study evaluating 107 patients who underwent TAR with FET endoleak was the second main indication for reintervention [5]. The incidence of this treatable FET complication has been reported to be ranging from 11% to 35%. Importantly, untreated endoleak negatively influences the aortic remodeling process by contributing to constant AL expansion. Therefore, the FET stent-graft size and length must be selected carefully after

accurate measurement [9, 10, 46, 81]. Kandola et al. [46] noted that 77% of patients with endoleak or sac expansion had < 10% of distal stent oversizing whilst the remaining 23% had less than 30 mm distal seal in the healthy portion of the aorta despite adequate oversizing. Stents of appropriate oversizing and sealing were significantly more commonly deployed in patients with no endoleak or sac expansion (P = 0.0031) [46]. In the present review, the pooled estimate of endoleak was calculated as 3% with a high heterogeneity which disappeared among patients receiving Thoraflex Hybrid in European centers. The study by Berger et al. [77] reported 0% endoleak incidence in the Thoraflex Hybrid group of patients whilst 3% of patients receiving the E-Vita HP developed endoleak. Another study reporting a 0% incidence of endoleak is the aforementioned Chu et al. [52]. On the contrary, Tsagakis et al. [83] found that 4.6% of patients experienced endoleak with the E-Vita device. To further demonstrate Thoraflex Hybrid's outstanding efficacy, Tan et al. [10] analyzed data from 931 patients who underwent FET using Thoraflex Hybrid and reported only 1 (0.1%) case of endoleak over a follow-up period of 84 months. In addition, the authors stated that the proximal sewn graft of Thoraflex Hybrid, combined with its distal anastomosis cuff, eliminate the risk of endoleak. Overall, the freedom from adverse events at 84 months after Thoraflex Hybrid implantation was 94%. All the above evidence show beyond doubt that the Thoraflex Hybrid is the best aortic arch prosthesis on the global market.

There is a clear trend within the literature associating the incidence of dSINE and endoleak with aortic remodeling. In addition, FET graft size and length have been strongly linked to these outcomes. This topic has been discussed in detail by Jubouri et al. [9] and Kayali et al. [81]. Research evidence has demonstrated that severe graft oversizing increases the likelihood of dSINE occurring which, in turn, negatively affects aortic remodeling, while at the same time independently causing negative remodeling [9, 10, 59]. On the other hand, stent graft undersizing may cause endoleak, which also hinders the remodeling process. Therefore, graft oversizing by 10-15% is recommended [75, 84, 85]. However, the optimal graft length remains debatable as longer grafts have been shown to promote improved remodeling and lower dSINE occurrence while increase the risk of SCI [9]. In this sense, Ma et al. [82] recommend using tapered stent grafts in order for them to be harmonious with the tapering nature of the descending aorta, thus preventing size mismatch and, consequently, dSINE, endoleak and negative remodeling. The Thoraflex Hybrid is a highly versatile and unique device as it is the only FET HP offering a wide range of proximal and distal stent-graft diameters as well as multiple device lengths which clearly explains its superior results achieved [9, 10, 59, 82].

5. Conclusion

The present meta-analysis of 5068 patients with TAAD and/or thoracic aortic aneurysm undergoing FET procedure provides a clear understanding of the incidence of FET complications, including negative aortic remodeling, dSINE and endoleak. These events may necessitate secondary endovascular intervention, thus minimizing their incidence is ideal. Therefore, the choice of FET graft type, size and length must be taken with great care. In addition, patients' clinical/anatomical characteristics should be seriously taken consideration. Nevertheless, Thoraflex Hybrid can be considered the primary FET device choice due to its superior results. Finally, in our results the type of stent-graft and the study location were sources of heterogeneity, emphasizing the need for multicenter studies directly comparing FET grafts.

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Figure legends

Figure 1. Study PRISMA flow chart

Figure 2. Pooled estimation of patients with postoperative dSINE

Figure 3. Pooled estimation of patients with postoperative endoleak

Figure 4. Pooled estimation of patients with postoperative endovascular treatment after FET procedure

Figure 5. Pooled estimation of patients with postoperative in-hospital mortality

Figure 6. Pooled estimation of patients with postoperative paraplegia

Figure 7. Pooled estimation of patients with postoperative renal failure

Figure 8. Pooled estimation of patients with postoperative cerebrovascular events

Figure 9. Pooled estimation of patients with postoperative 30-day mortality

Supplemental Figure 1. Pooled estimation of patients with postoperative FLT at the level of (A) stent-graft, (B) thoracic aorta, and (C) abdominal aorta

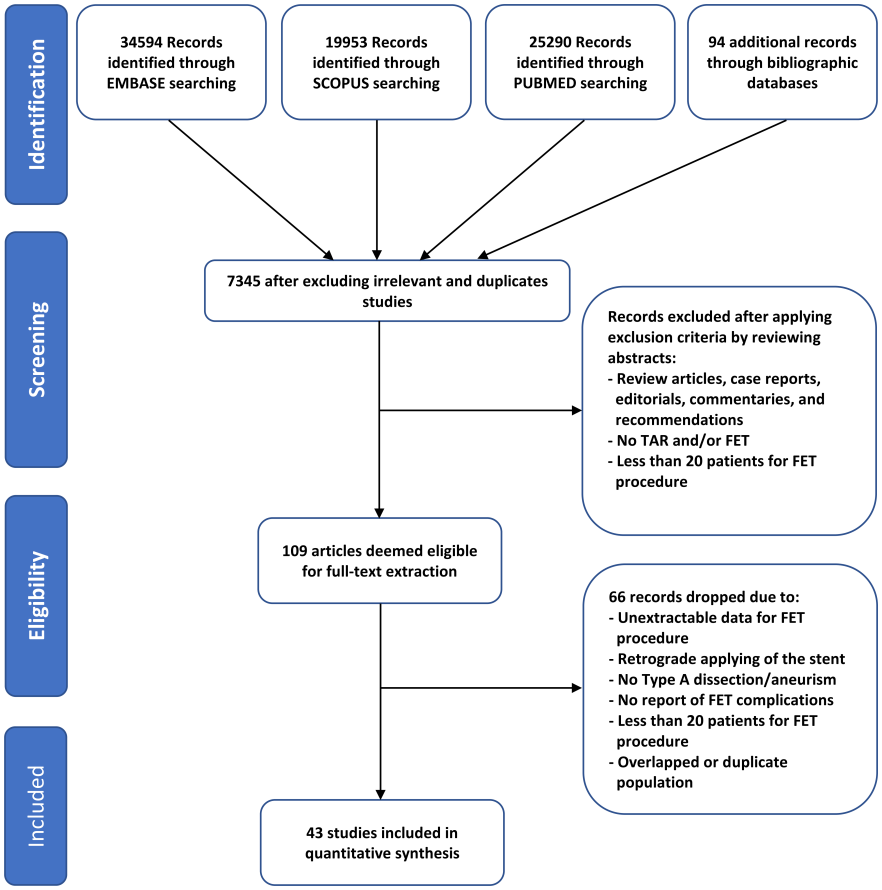
Supplemental Figure 2. Funnel plots showing publication bias for (A) dSINE, (B) endoleak, (C) endovascular treatment after FET procedure, (D) FLT at stent-graft level, (E) FLT at thoracic aorta level, (F) FLT at abdominal aorta level, (G) in-hospital mortality, (H) paraplegia, (I) renal failure, (J) cerebrovascular events, and (K) 30-day mortality

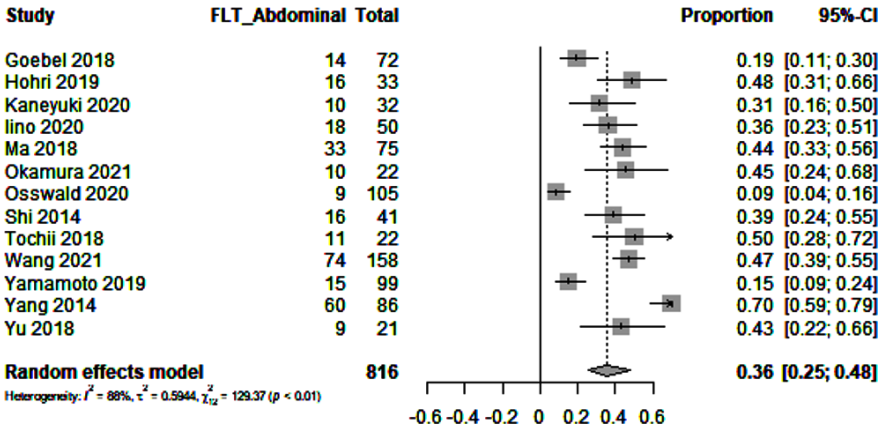
Tables

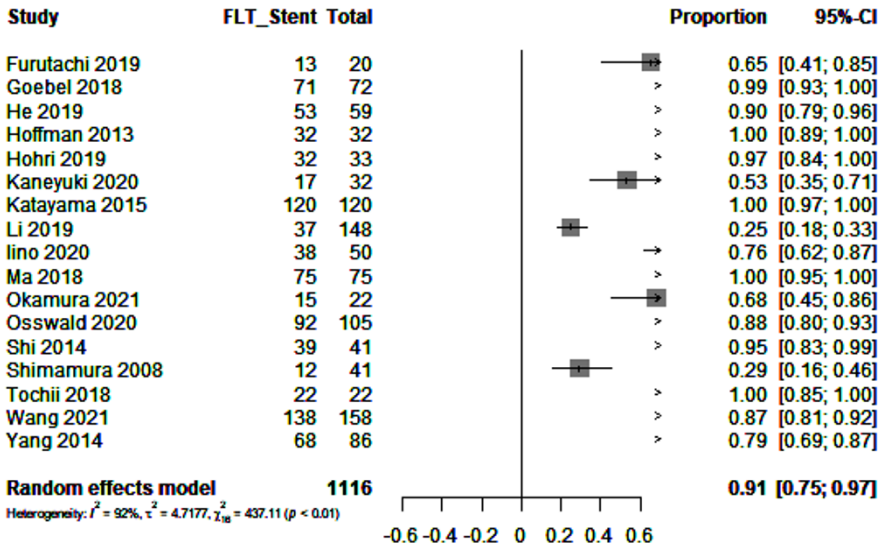
Table 1. Summary of baseline characteristics and procedural features

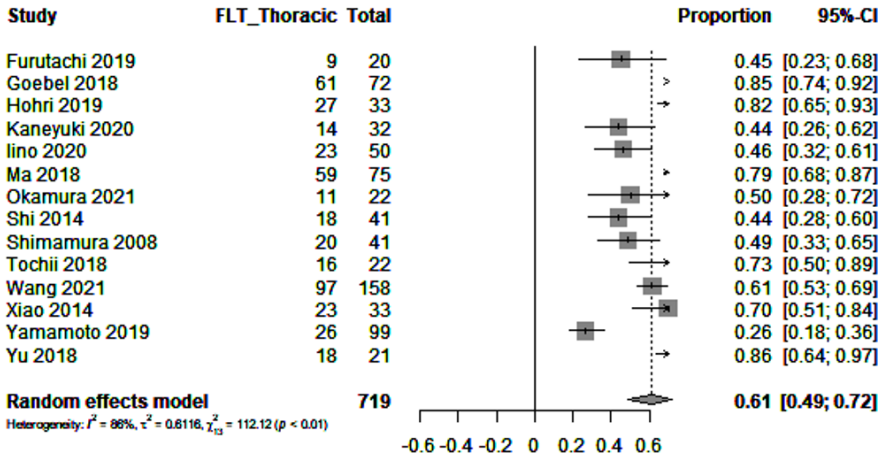
Table 2. Subgroup analyses showing changes in the estimates of postoperative outcomes and heterogeneity

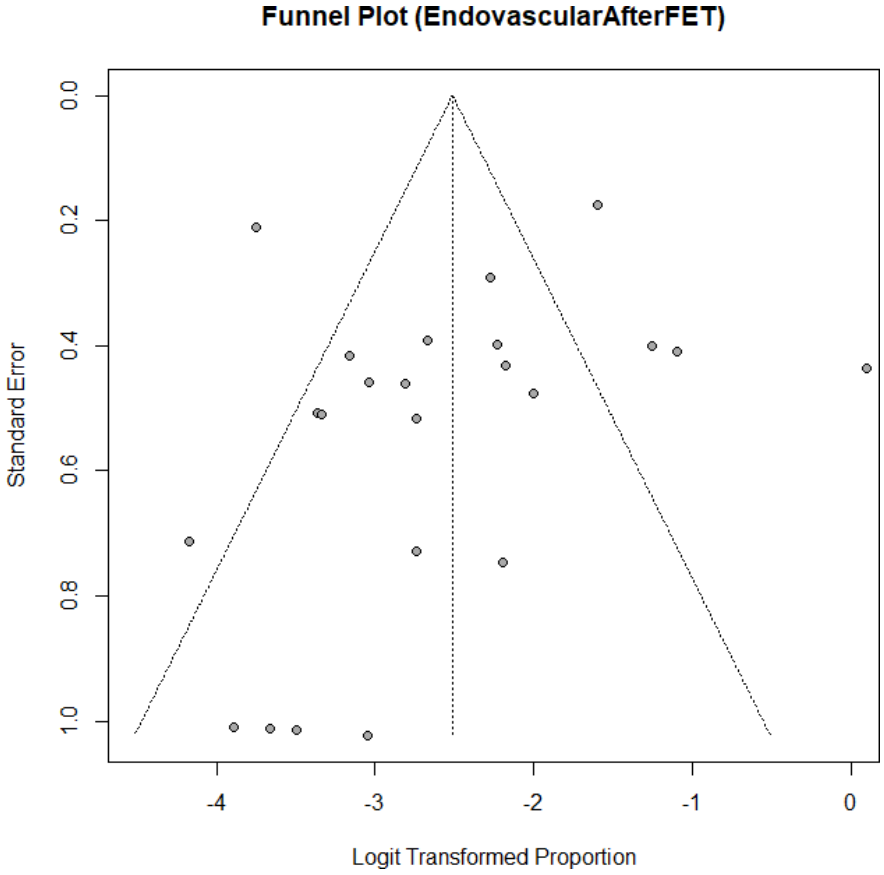
Supplementary Table 1. Keywords used in database searching

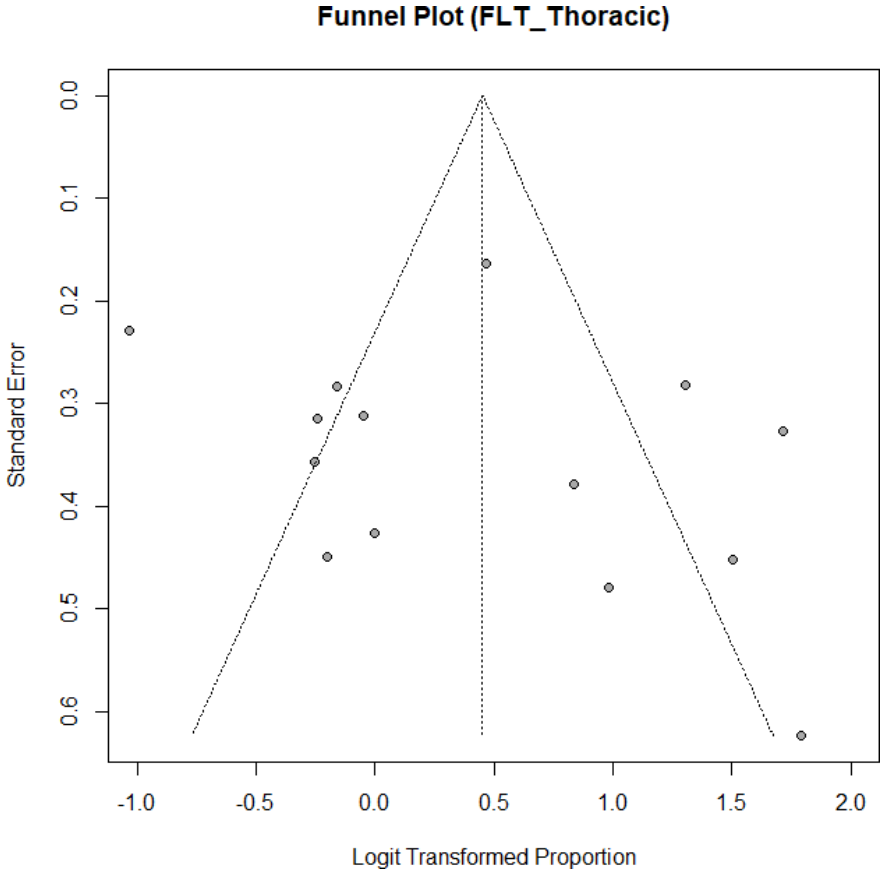


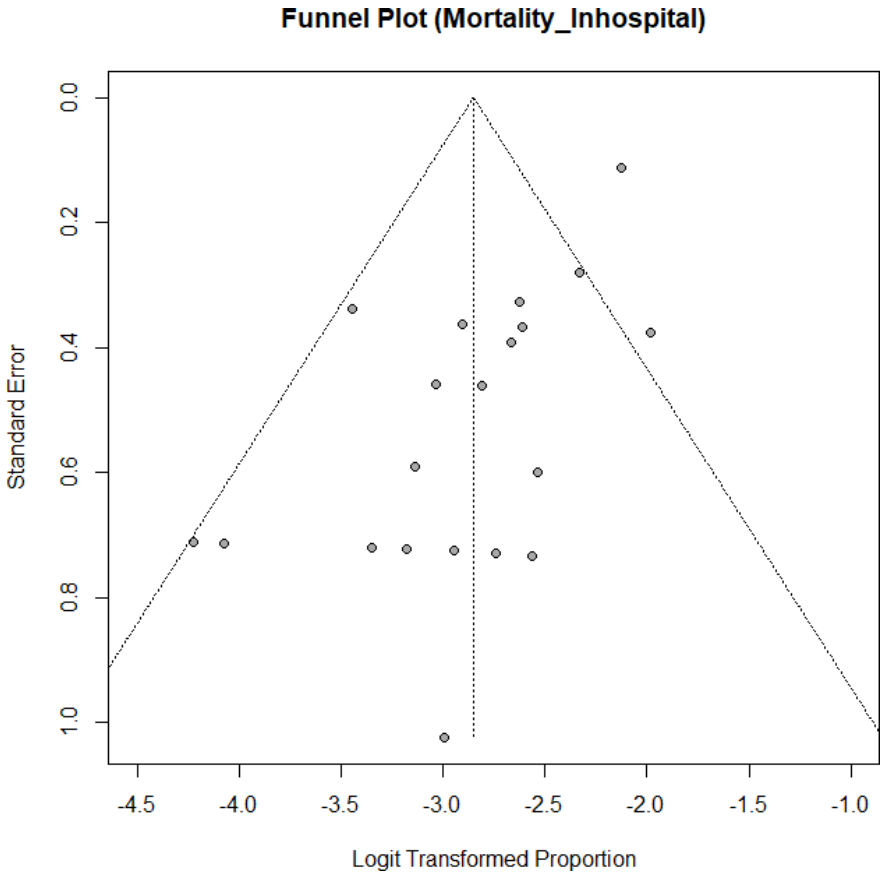


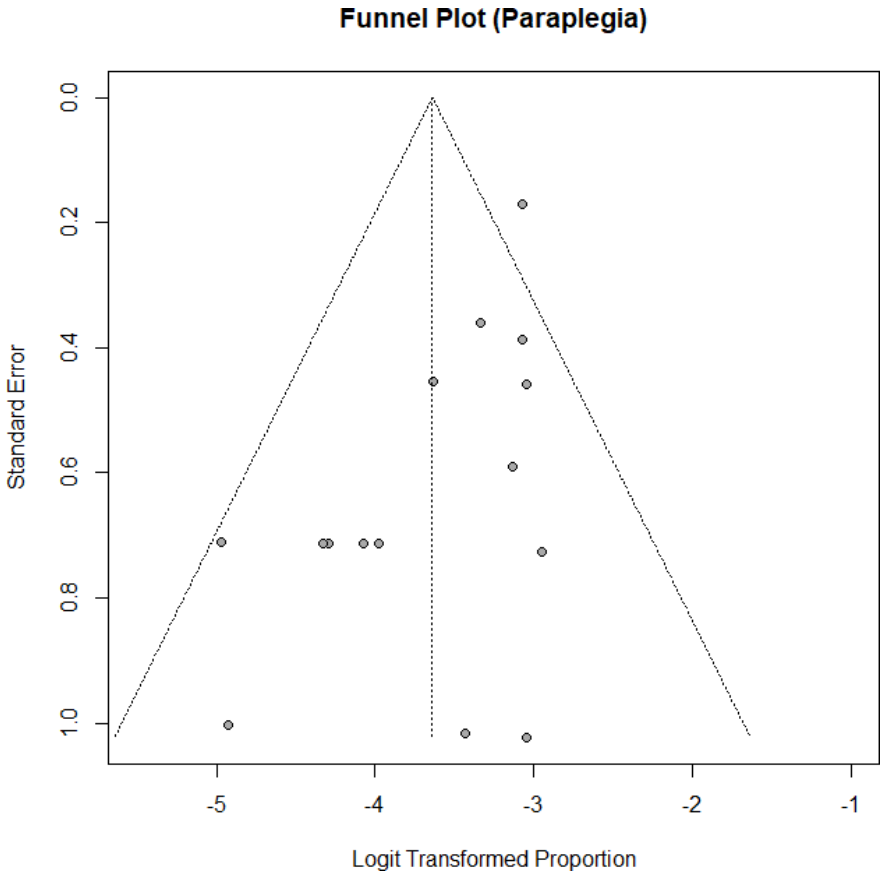


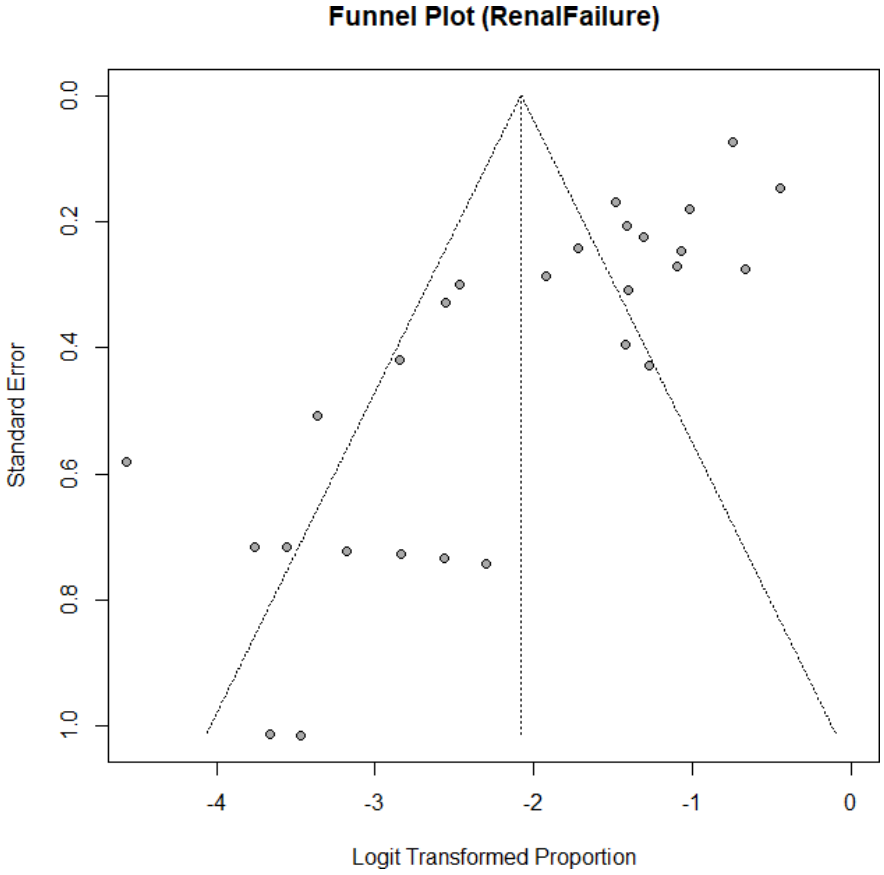


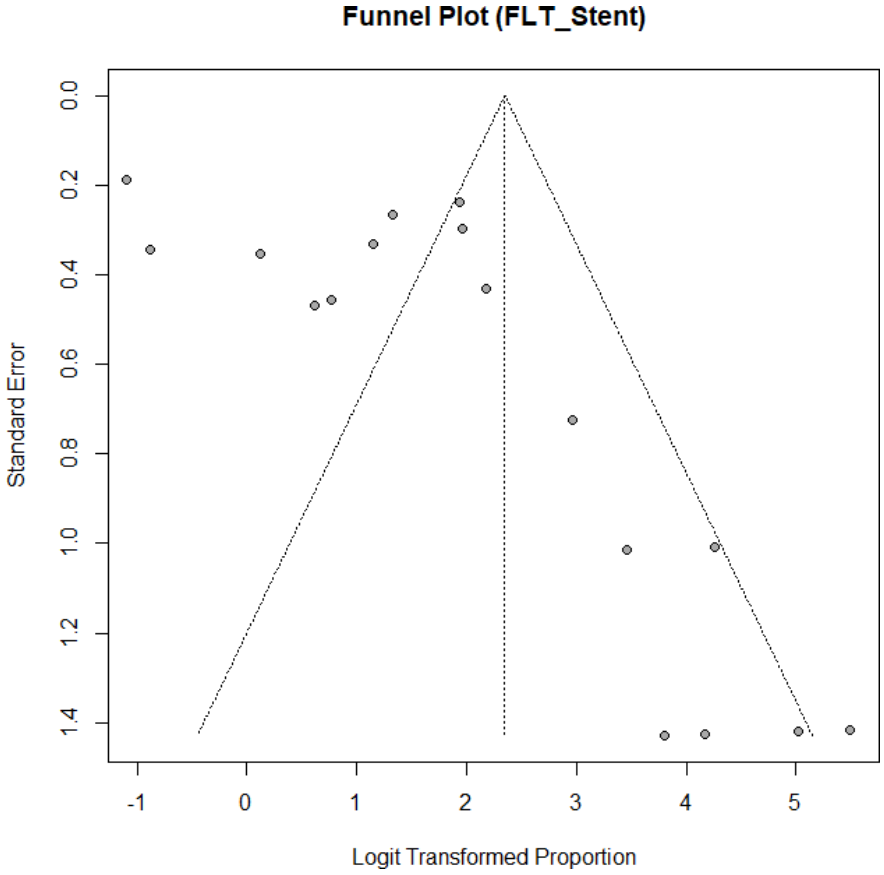


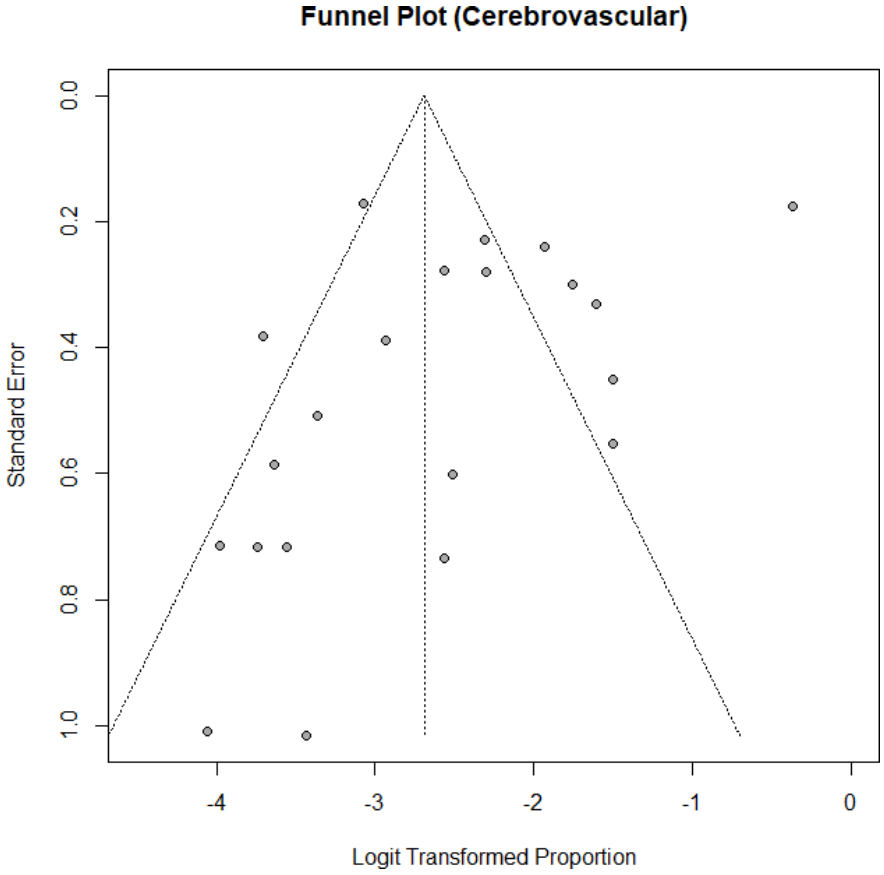


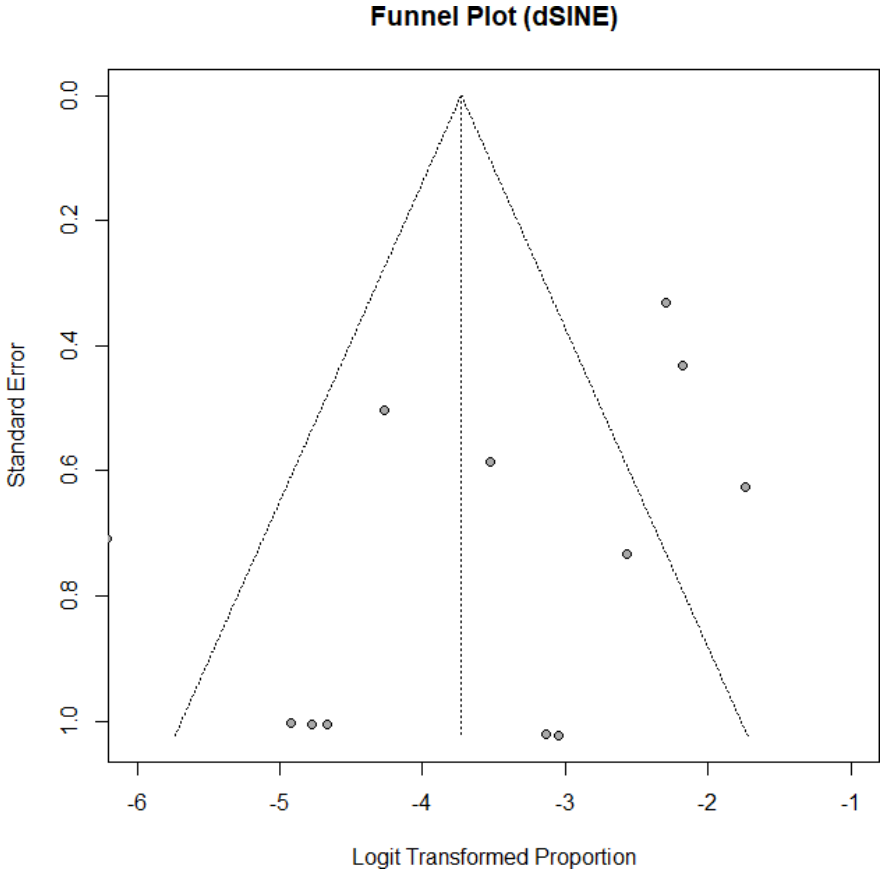


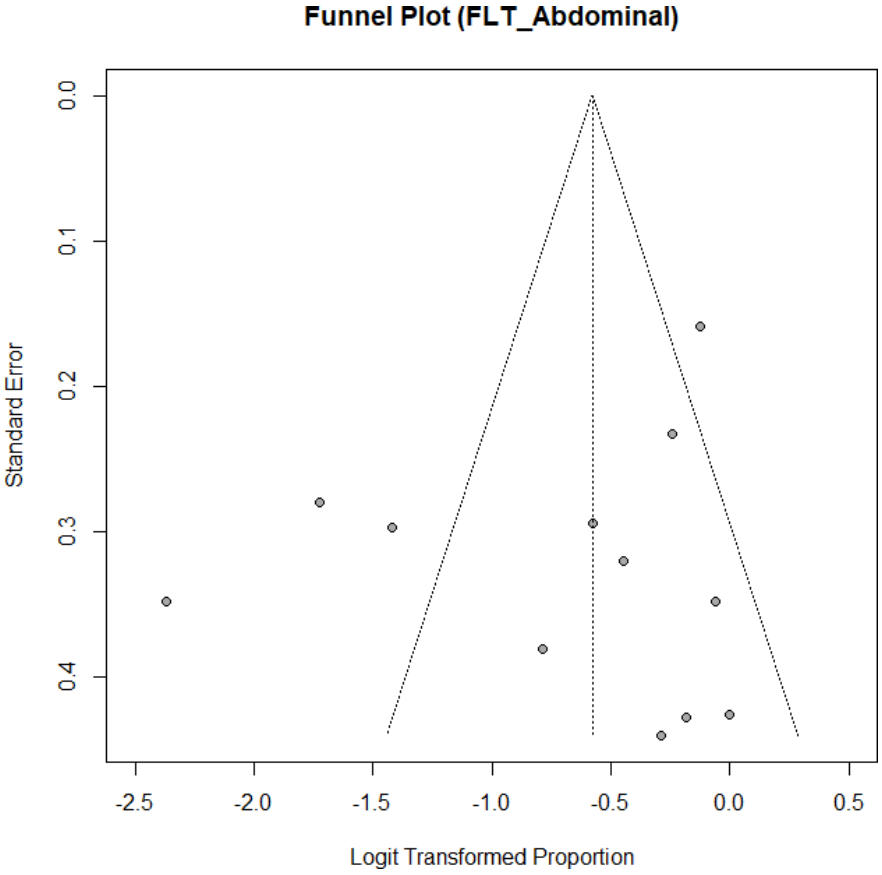


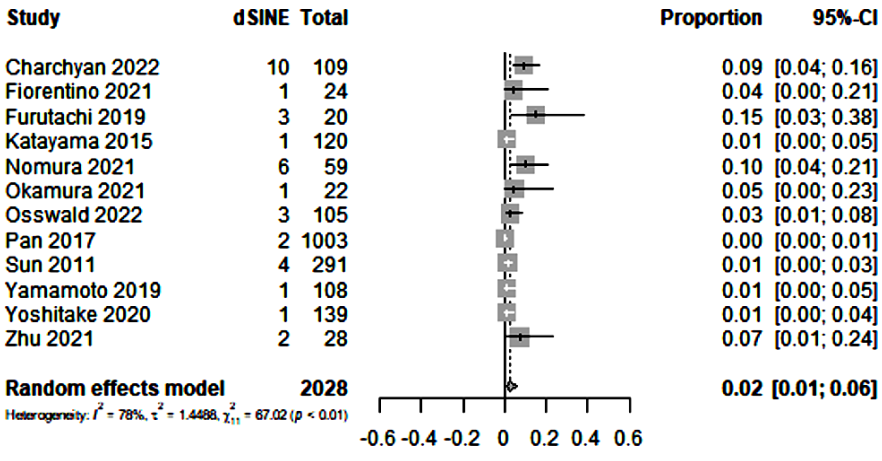


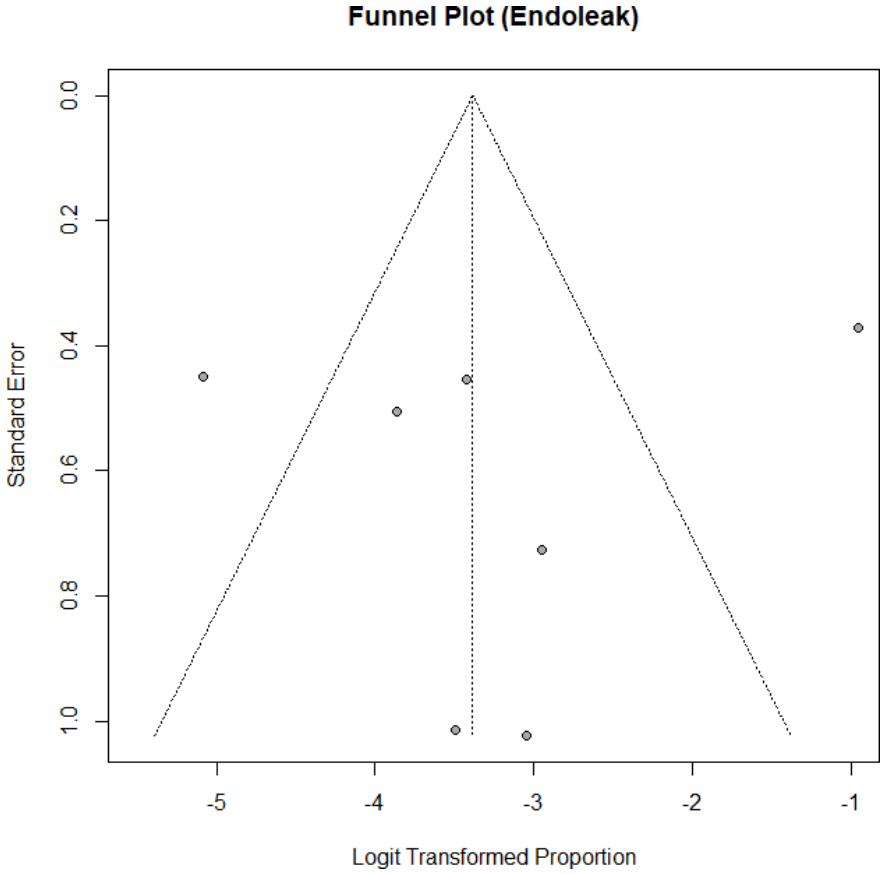


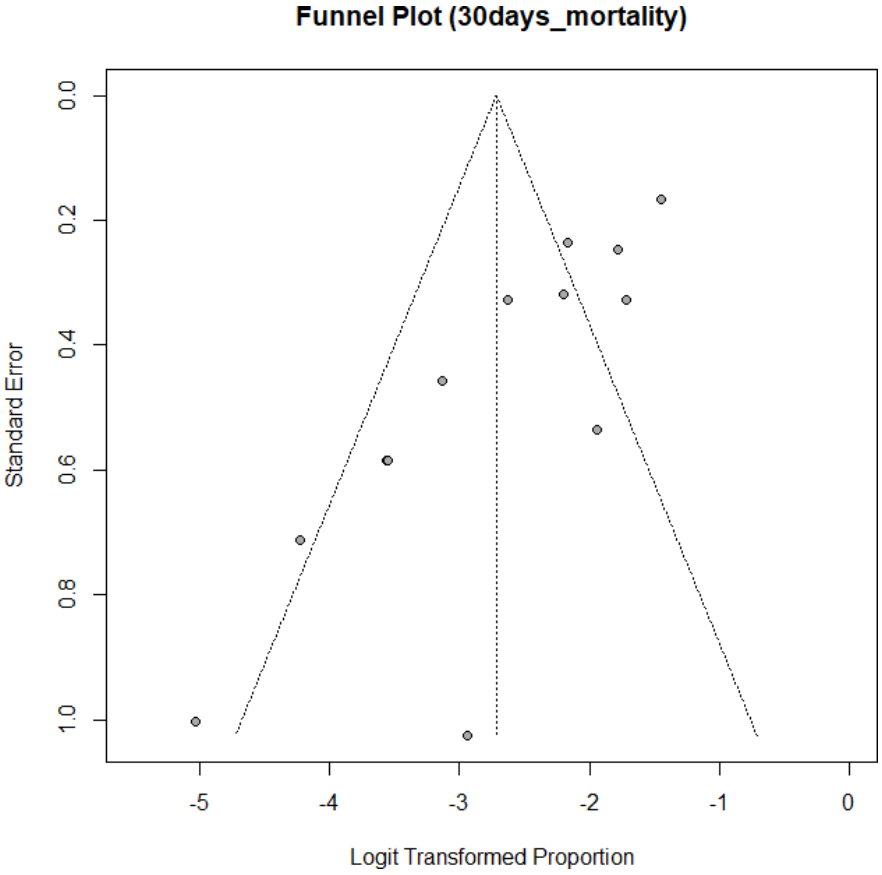


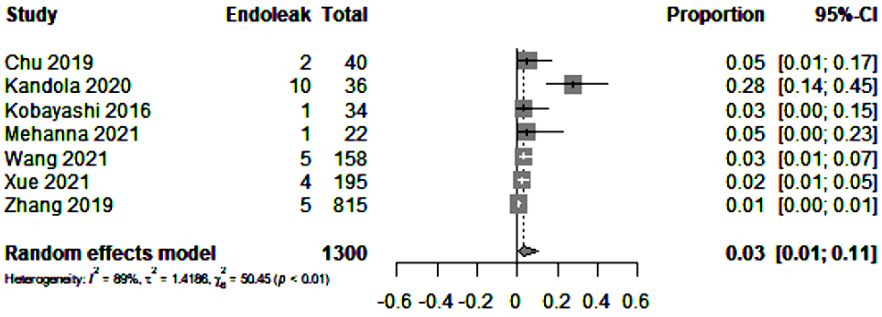


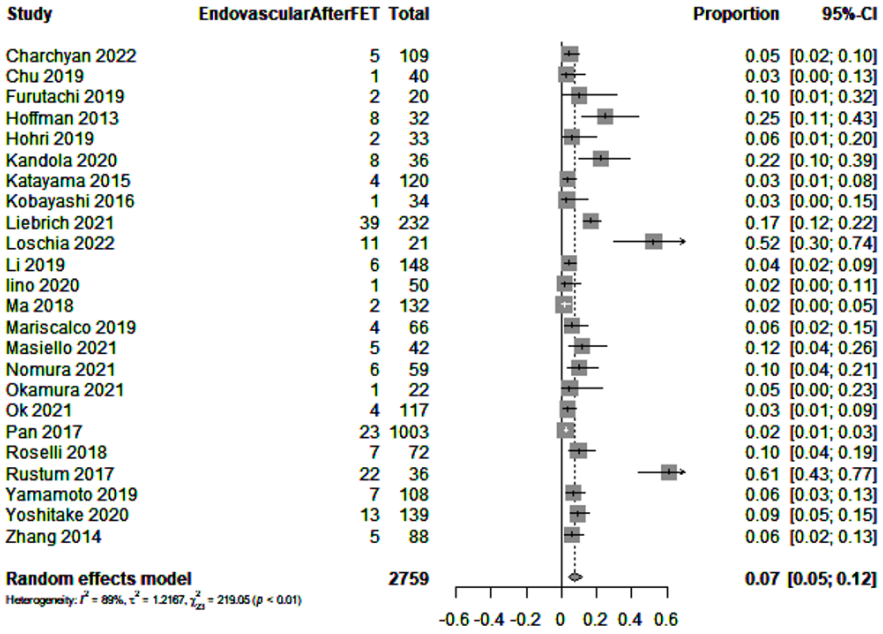


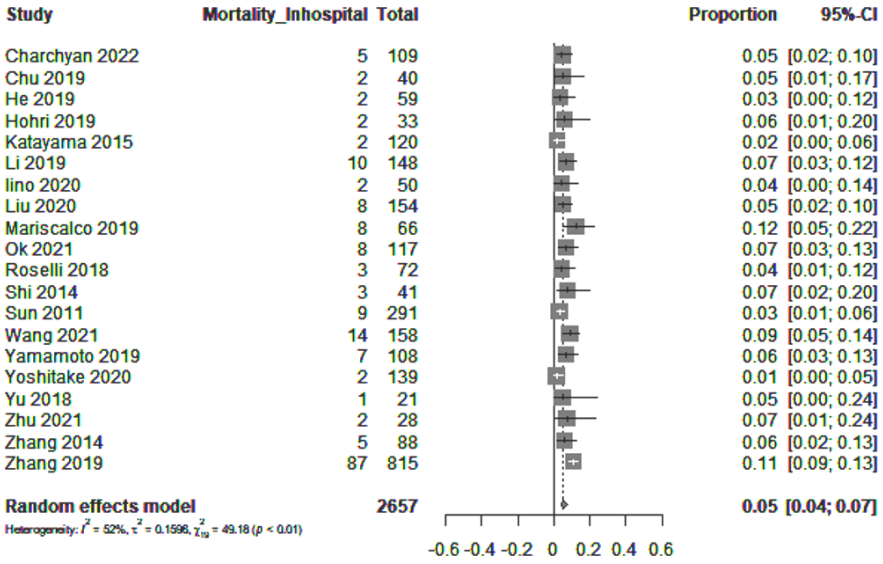


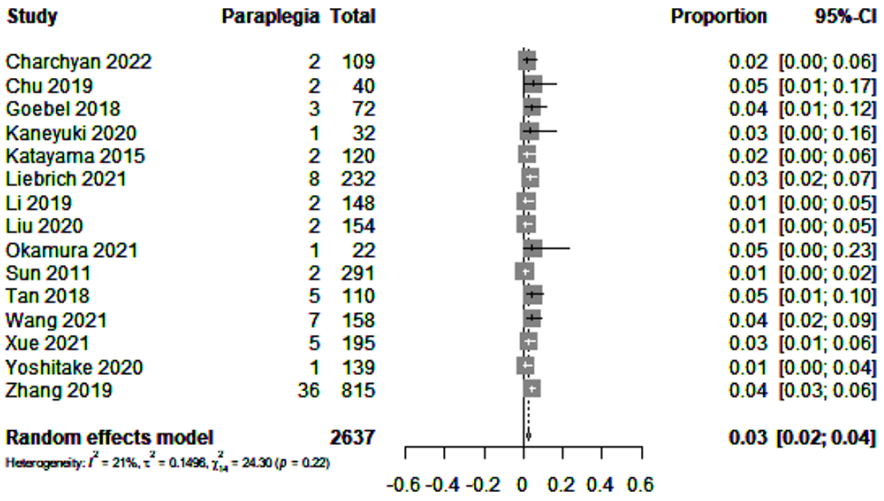


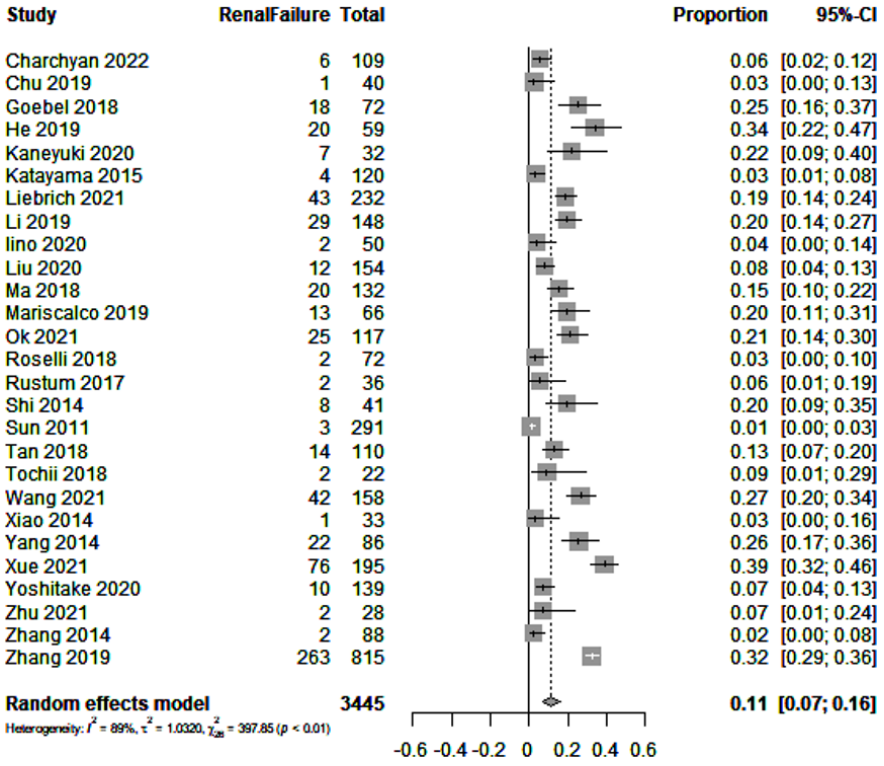


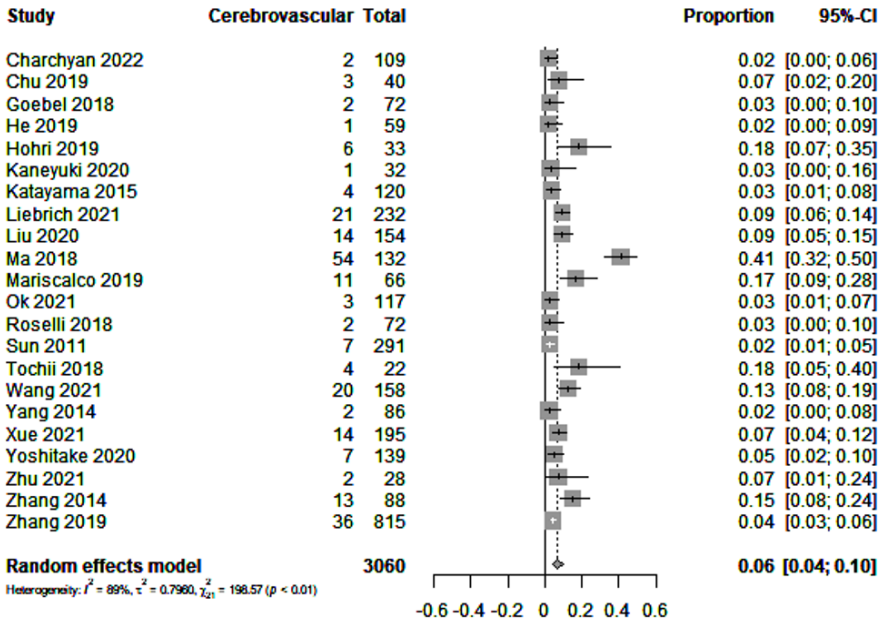


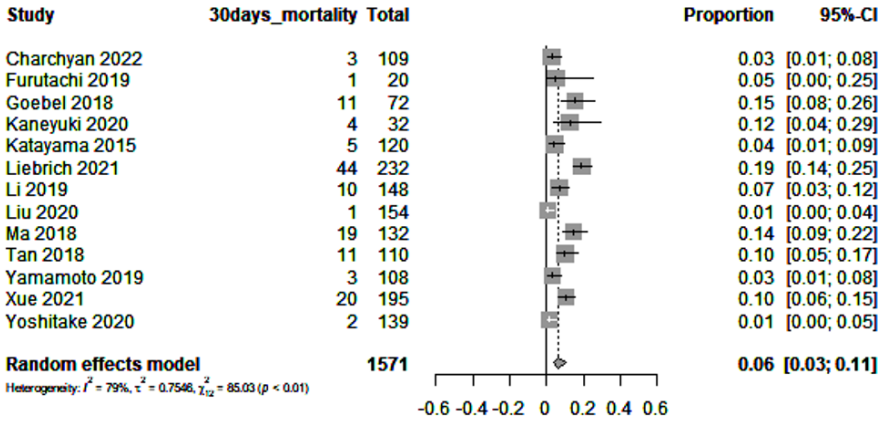












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