The safety and efficacy of the LAmbre left atrial appendage closure device in atrial fibrillation: a systematic review and meta-analysis

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Abstract

The LAmbre occluder is more convenient to operate than other left atrial appendage closures(LAAC), and it can adapt to different anatomy of left atrial appendage. However, some studies showed that Lambre occluder had a higher incidence of device-related thrombus(DRT). This meta-analysis aims to compare the safety and efficacy of the LAmbre occluder with other LAAC devices. Eligible studies were retrieved from PubMed, Embase and the Cochrane Library up to 1 July 2022 and reported the results. Five studies of a total of 607 patients were included in the meta-analysis. The LAmbre occluder was associated with higher rate of DRT(OR [95% CI] = 5.25 [1.21, 22.86], P =0.03; I2=0%). No significant differences were observed in the incidence of procedure-related death, pericardial effusion, chest pain, bleeding and vessel complication, contrast medium, fluoroscopy time ,death, stroke, bleeding events, systemic embolism and peri-device leakage. In conclusion, the LAmbre occluder had higher incidence of DRT than other LAAC devices, and there were no significant differences in stroke, bleeding events, and mortality.

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Abstract

The LAmbre occluder is more convenient to operate than other left atrial appendage closures(LAAC), and it can adapt to different anatomy of left atrial appendage. However, some studies showed that Lambre occluder had a higher incidence of device-related thrombus(DRT). This meta-analysis aims to compare the safety and efficacy of the LAmbre occluder with other LAAC devices. Eligible studies were retrieved from PubMed, Embase and the Cochrane Library up to 1 July 2022 and reported the results. Five studies of a total of 607 patients were included in the meta-analysis. The LAmbre occluder was associated with higher rate of DRT(OR [95% CI] = 5.25 [1.21, 22.86], P =0.03; I2=0%). No significant differences were observed in the incidence of procedure-related death, pericardial effusion, chest pain, bleeding and vessel complication, contrast medium, fluoroscopy time ,death, stroke, bleeding events, systemic embolism and peri-device leakage. In conclusion, the LAmbre occluder had higher incidence of DRT than other LAAC devices, and there were no significant differences in stroke, bleeding events, and mortality.

Introduction

Atrial fibrillation (AF) is the most common persistent arrhythmia seen in clinical practice, and it is a leading cause of morbidity and mortality from cardioembolic stroke, which accounts for 15% to 20% of all ischemic strokes.[1,2] The incidence of ischemic stroke among patients with nonvalvular AF (NVAF) is approximately 5% per year, a 5.6-fold increase when compared with an age-matched population in sinus rhythm.[3,4] There are numerous published studies in stroke prevention showed that oral anticoagulation(OAC) is common and effective in preventing stroke in people with AF.[5-10] However, it is often underused due to poor patient adherence, contraindications and potential bleeding complications.

More than 90% of atrial thrombi in patients with NVAF are found in the left atrial appendage(LAA), according to autopsy and echocardiography investigations.[11,12] This makes it possible to the application of left atrial appendage closure (LAAC) as an alternative to OAC for the prevention of stroke in patients with AF. Percutaneous LAAC has been demonstrated to be beneficial in preventing stroke in individuals with AF in numerous investigations.[13-17] The most frequently used LAAC devices are the Watchman (Boston Scientific, Marlborough, MA) and Amplatzer occluders (Abbott, St Paul, MN). The Amplatzer occluders include the Amplatzer cardiac plug (ACP) and the Amulet. Both the Watchman[18-20] and the Amplatzer[17,21,22] occluders have been tested in multiple clinical studies to verify their effectiveness in preventing stroke, bleeding events, and reducing cardiovascular death. Whereas, both of them had relatively large delivery sheaths (9–14 French) , and the recapture and repositioning capability of them is limited. In June 2016, the LAmbre occluder (LifeTech Scientific, Shenzhen, China) got the CE certification. It has a broader range of sizes and an adjustable sheath than other LAAC devices, allowing it to accommodate various LAA anatomy. Meanwhile, it also has a recyclable design to further improve the success rate of implantation.[23,24]

Some studies compared the clinical outcomes of the LAmbre occluder to those of other LAAC devices, which with contradictory results. The LAmbre occluder had a higher rate of device-related thrombus(DRT) than other LAAC devices, according to Schnupp et al.[25] and Chen et al.[26], whereas Litwinowicz et al.[27] found the opposite. The goal of this study was to compare the safety and efficacy of the LAmbre occluder to that of other LAAC devices.

Methods

Study inclusion and exclusion criteria

Citations were screened at the title and abstract level and retrieved as full reports. The inclusion criteria were: (1) comparison of the LAmbre occluder versus other LAAC devices; (2) studies reporting at least one of the safety outcomes or efficacy outcomes. All RCTs and observational studies that fulfilled the inclusion criteria were included.

The exclusion criteria: (1) a duplication of previous publications; (2) a comment, review or editorial; and (3) a study without data. The studies were independently selected by two investigators, according to the inclusion and exclusion criteria by screening the title, abstract and full-text. Any dispute was resolved by discussion.

Data extraction

From each study, the following data were independently extracted by the first two investigators using a standardized form: first author's last name, year of publication, journal, LAmbre occluder, other LAAC devices, sample size, age, gender, patients with paroxysmal AF, patients with non-paroxysmal, CHA2DS2-VASc score(congestive heart failure, hypertension, age 75 years or older [doubled], diabetes, stroke [doubled], vascular disease, age 65 to 74 years, sex category [female]), HAS-BLED score(hypertension, abnormal renal/liver function, stroke, bleeding, labile international normalized ratio, elderly, and drugs/alcohol), patients with heart failure, patients with hypertension, patients with diabetes, patients with previous stroke/TIA/systemic embolism, patients with prior major bleeding, patients with peripheral vascular disease, patients with coronary artery disease, patients with liver/renal dysfunction, patients with labile INR, anti-thrombotic medical therapy before LAAC, and average follow-up. For data from multiple treatment groups, the approach recommended in the Cochrane handbook was adopted to avoid a unitof –error analysis that may result from entering several comparisons into one meta-analysis, which could lead to "double-counts" of patients based on the same study. Disagreements were resolved through discussion.

Study outcomes and definitions

The safety outcomes included implant success, procedure time, fluoroscopy time, total contrast medium, pericardial effusion, chest pain, access vessel complication and procedure/device-related death or bleeding. The efficacy outcomes included death, stroke, bleeding events, systemic embolism, peri-device leakage and device-related thrombus. Definitions of safety outcomes and efficacy outcomes are described in the Table 2.

Statistical analyses

Review Manager (RevMan5.4.1, The Cochrane Collaboration, Oxford, UK) and Stata 16.0 were utilized for meta-analyses. All outcomes in this study were categorical data and the results were expressed as odds ratio (OR) with 95% confidence intervals (CI). Heterogeneity was assessed using the I^2 statistic, with values <25%, 25–50%, >50% indicating low, moderate, and high heterogeneity respectively. Pooled analyses were calculated using fixed-effect models (Mantel-Haenszel method), whereas random-effect models (Der Simonian and Laird method) were applied if I^2 >50%. Publication bias was estimated visually by funnel plots. All tests were two-sided and P[?]0.05 was considered statistically significant.

Results

Characteristics of the Included Studies:

Three hundred and nine articles were obtained by online and manual searches. After removing duplicates, screening titles and abstracts, four independent trials[25-28] contained data for the LAmbre occluder versus other LAAC devices were selected that included 607 patients (142 randomized to the LAmbre occluder and 465 to other LAAC devices). (Figure 1) (as seen in the flow chart).

Study characteristics

The characteristics of the trials and patients are shown in Table 1. In these trials compared the LAmbre occluder with the Watchman occluder, the Amplatzer occluders (ACP and Amulet device) and the Lariat occluder (SentreHEART Inc, Redwood, CA). The majority of the participants were men, with an average age of over 65 years. The person of these trials had some underlying medical conditions such as: hypertension, heart failure, diabetes, stroke and so on, consequently average CHA2DS2-VASc score ranged from 3.5 to 5.0, average HAS-BLED score ranged from 2.3 to 4.1. All trials were followed up for more than six months, during postoperative follow-up, transesophageal ultrasonography was conducted. As showed in Schnupp et

al.[25] and Litwinowicz et al.[27], before the left atrial appendage procedure, most of the patients were given anticoagulant treatment, while a few were given antiplatelet therapy.

Safety outcomes

As we observed, both the LAmbre occluder and other LAAC devices had high implant success rate. In particular, the LAmbre occluder had 100 percent success rate in three studies. [25-27] However, there was no significant statistical difference between the LAmbre occluder and other LAAC devices in implant success rate (OR [95% CI] = 1.13 [0.25, 5.10], P =0.88). This meta-analysis found no vital variations within procedure-related death, pericardial effusion, chest pain, bleeding and vessel complication, contrast medium and fluoroscopy time (Table 3).

Efficacy outcomes

Three studies contributed to the analysis of DRT. Compared with other LAAC devices , the LAmbre occluder had a significantly higher rate of DRT (OR [95% CI] = 5.25 [1.21, 22.86], P =0.03; I^2=0%). No significant differences were observed in the incidence of death, stroke, bleeding events, systemic embolism and peri-device leakage (Table 4).

Discussion

With the increase of age, the incidence of atrial fibrillation gradually increases, some patients have advanced age, ineffective anticoagulation and anticoagulation contraindications, which bring difficulties to the prevention and treatment of thromboembolic events. For elderly patients at high risk of stroke, LAAC can replace anticoagulant therapy in patients with non-valvular AF, effectively prevent thromboembolic events and reduce anticoagulation-related bleeding events. Many previous studies have proved the safety and efficacy of the LAAC devices. Our meta-analysis first compared the safety and efficacy of the LAmbre occluder with other LAAC devices. There were no significant differences in the risk of implantation success, procedure-related complications, bleeding events, death, or stroke between the LAmbre occluder and other LAAC devices, but the LAmbre occluder had higher risk of DRT than other LAAC devices.

The LAmbre occluder is simpler for operator than other LAAC devices, it not only has a higher implant success rate (OR [95% CI] = 1.13 [0.25, 5.10], P =0.88), but also has less procedure time (OR [95% CI] = -0.27 [-1.83, 1.29], P =0.73), less fluoroscopy time (OR [95% CI] = -0.54 [-1.42, 0.34], P =0.23) and less contrast medium (OR [95% CI] = -6.50 [-24.28, 11.28], P =0.47). This is due to that the LAmbre occluder had several sizes (16–36 mm) to accommodate the variation of LAA anatomy and they were delivered by sheaths that ranged 8–10 French in size.[24] Meanwhile, it had full recapture and repositioning capabilities.

There was one procedure-related death case in this meta-analysis. Schnupp et al. reported a case of left atrial appendage perforation caused by guidewire in the LAmbre group, who died of multiorgan failure 3 days after surgery[25]. This complication was not caused by the device itself but related to the procedure. At the same time, there were only two studies reported procedure-related death.[25,26] The final results showed no significant difference between the two groups (OR [95% CI] = 10.40 [0.38, 286.38], P =0.17; I^2=0%).

Pericardial effusion and major bleeding are also serious procedure-related complications that may threaten patients' life, and we found there were no significant differences in pericardial effusion (OR [95% CI] = 1.04 [0.30, 3.62], P =0.95; I^2=2%) and major bleeding OR [95% CI] = 1.93 [0.35, 10.75], P =0.45; I^2=0%) in this meta-analysis.

Transesophageal echocaridoraphy(TEE) was used to evaluate the occurrence of peri-device leakage(>5mm) and DRT. There were two studies involved peri-device leakage data,[25,26] the result showed that there was no significant difference between the LAmbre occluder and other LAAC devices(OR [95% CI] = 2.43 [0.25, 23.87], P =0.45; I^2=0%). Three studies contributed to the analysis of DRT.[25-27] Compared with other LAAC devices, the LAmbre occluder had higher rate of DRT(OR [95% CI] = 5.25 [1.21, 22.86], P =0.03; I^2=0%). There were four cases with DRT in the LAmbre group, three of them were reported by Schnupp et al..[25] The final angiography of these three cases at the end of the intervention revealed a small peri-device leak <5

mm at the ridge to the left pulmonary veins. Furthermore, in one of those cases, the device was implanted deep into the ostium. Therefore, with the improvement of operator techniques, the incidence of DRT in the LAmbre occluder may decrease significantly. In contrast, one case with DRT in the Amplatzer group, which occurred on a device that completely sealed the ostium of the LAA.[25] During this time, with the exception of one patient with DRT had a non-disabling ischemic stroke in the LAmber group, others didn't have a stroke during the follow-up time.

We discovered that the LAmbre occluder had a significantly higher risk of stroke than other LAAC devices in the study by Litwinowicz et al., and this finding was statistically significant(OR [95% CI] = 8.95 [1.20, 66.76], P =0.03). It is not surprising that the LAmbre group had a higher incidence of stroke than the other LAAC group, because person in the LAmbre group were older(71.63±8.2 vs 65.0±10.6), over half of the population had a previous stroke(54.2% vs 28.6%). Meanwhile, the incidence of other underlying diseases in the LAmbre group was also higher compared with other LAAC group, such as heart failure(37.5% vs 21.6%), hypertension(100% vs 95.5%), diabetes(37.5% vs 27.1%). Therefore, the CHA2DS2-VASc score in the LAmbre group was higher than that in other LAAC group(5.0±1.5 vs 4.1±1.8), which was confirmed by the result. In other studies,[26,28] the LAmbre group had relatively lower CHA2DS2-VASc score(Chen et al. 3.9±1.5, Wang et al. 4.1±1.5), consequently, the incidence of stroke was not elevated(Chen et al. 0%, Wang et al. 2.1%), and there was no significant difference with other LAAC group(Chen et al. OR [95% CI] =3.62 [0.07, 186.36], Wang et al. OR [95% CI] =1.02 [0.06, 16.81]). Therefore, the final result showed that the LAmbre occluder was not inferior in reducing the risk of stroke compared to other LAAC devices(OR [95% CI] = 3.36 [0.71, 15.81], P =0.13; I^2=0%).

During follow-up, twelve patients had bleeding events in this meta-analysis, two of them occurred in the LAmbre group, the final result was not statistically significant(OR [95% CI] = OR [95% CI] = 3.36 [0.71, 15.81], P =0.43; I^2=0%). All bleeding events were reported by Litwinowicz et al.(8.3% vs 5.0%, OR [95% CI] =1.72 [0.35, 8.35]). Higher HAS-BLED score may contribute to more bleeding events. The population of Litwinowicz et al. study and Chen et al. had higher HAS-BLED score than Wang et al. study(Litwinowicz et al. 4.0 +- 1.1 vs 3.9 +- 1.0, Chen et.al. 4.1 +- 1.0 vs 3.9 +- 1.1, Wang et al. 2.8 +- 1.0 vs 2.3 +- 0.9). Whereas, the follow-up time of Chen et al. study is only six months, so there may be less bleeding events.

Although the LAmbre occluder had a higher incidence of DRT, it did not significantly increase the incidence of stroke and bleeding, so there was no significant difference in mortality between the LAmbre occluder and other LAAC devices(OR [95% CI] = OR [95% CI] = 1.36 [0.49, 3.80], P =0.55; I^2=0%).

There were several limitations in this meta-analysis. First, only English language articles were included in our study, which may bias the results. Second, patient heterogeneity and confounding factors might have affected the analysis. Third, significant heterogeneity was detected in some pooled analyses, which may have affected the meta-analysis results, even though we adopted the random effects model or introduced sensitivity analysis. Fourth, the number of included studies was relatively small, and the results should be interpreted with caution, further studies are needed to confirm these results.

In conclusion, the LAmbre occluder had high implantation success rate, and fewer procedure-related complications. Although it had a higher incidence of DRT than other LAAC devices, it did not influence the incidence of stroke, bleeding events, and mortality.

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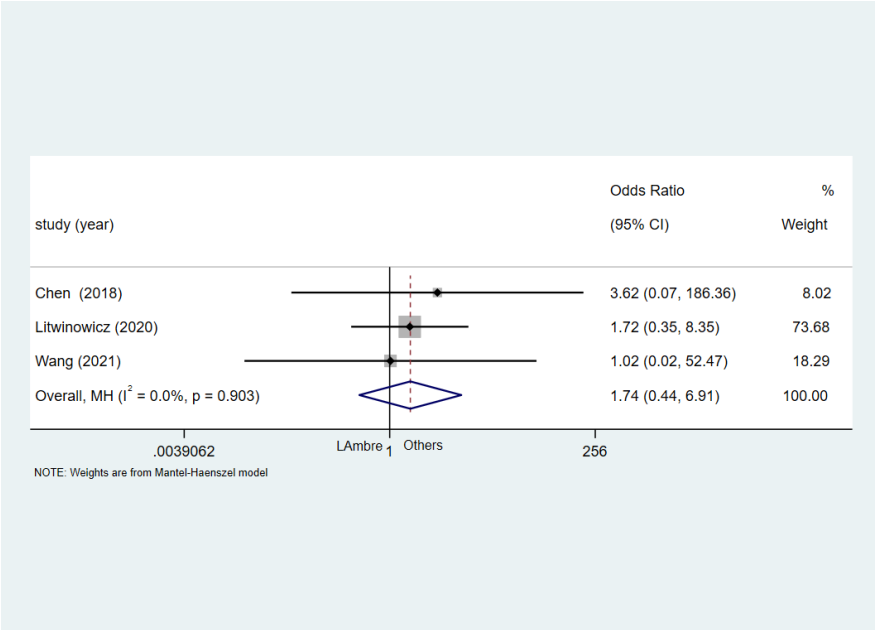
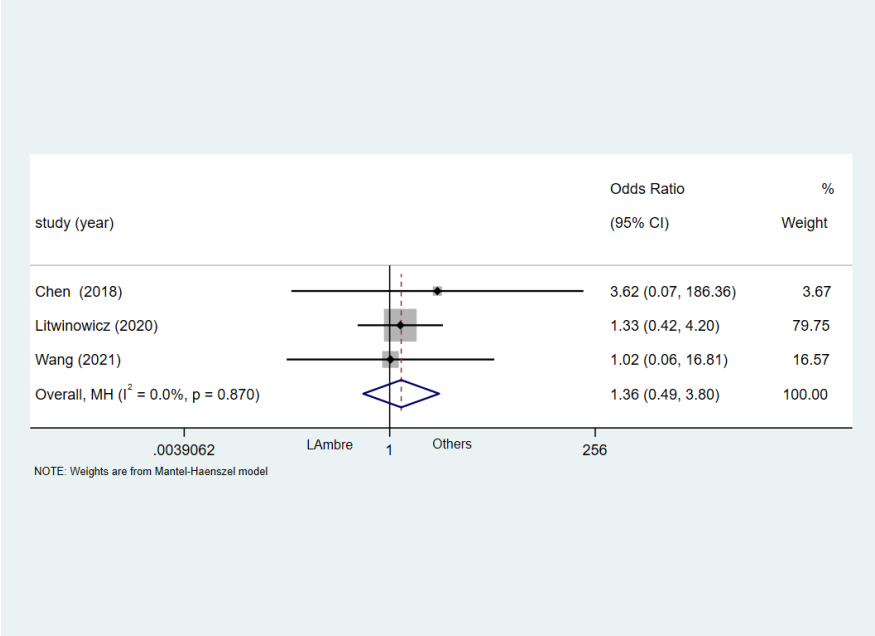
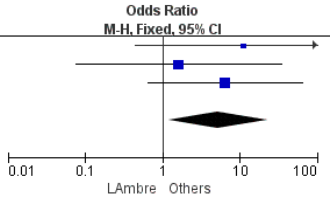




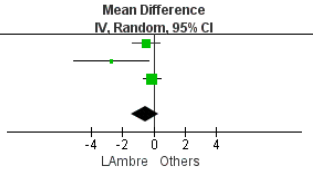
Study or Subgroup	LAmbre Events	LAmbre Total	Others Events	Others Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen 2018	1	30	0	110	15.2%	11.24 [0.45, 283.02]
Litwinowicz 2020	0	24	2	199	39.9%	1.61 [0.08, 34.57]
Schnupp 2020	3	36	1	72	44.8%	6.45 [0.65, 64.41]
Total (95% CI)		**90**		**381**	**100.0%**	**5.25 [1.21, 22.86]**
Total events	4		3			

Heterogeneity: Chi² = 0.81, df = 2 (P = 0.67); I² = 0%
Test for overall effect: Z = 2.21 (P = 0.03)



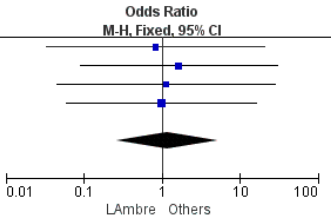
Study or Subgroup	LAmbre Mean	LAmbre SD	LAmbre Total	Others Mean	Others SD	Others Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2018	3.5	1.9	30	4	3.2	110	37.9%	-0.50 [-1.41, 0.41]
Schnupp 2020	12.8	4.9	40	15.5	9.8	107	11.1%	-2.70 [-5.10, -0.30]
Wang 2021	6.6	1.4	48	6.7	1.3	49	51.0%	-0.10 [-0.64, 0.44]
Total (95% CI)			**118**			**266**	**100.0%**	**-0.54 [-1.42, 0.34]**

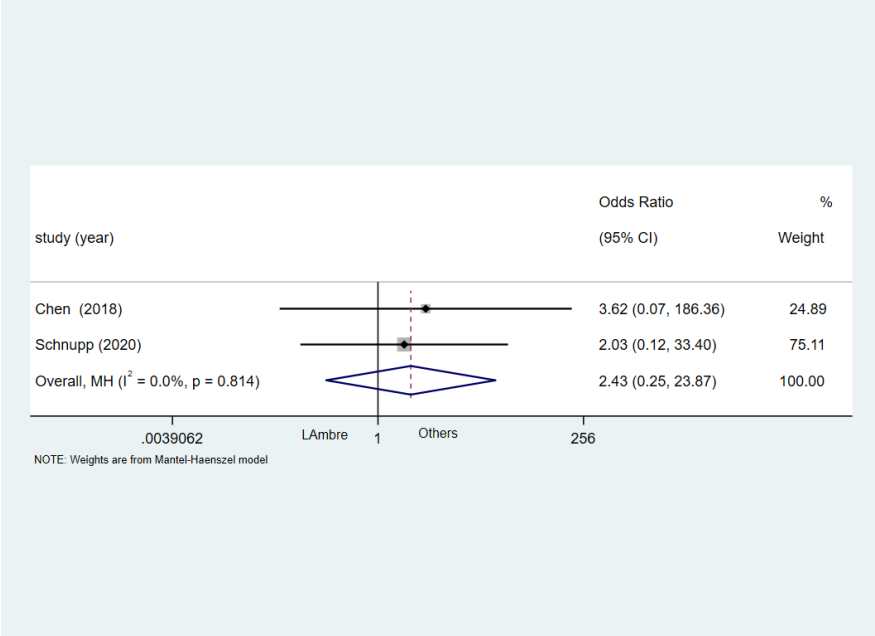
Heterogeneity: Tau² = 0.32; Chi² = 4.56, df = 2 (P = 0.10); I² = 56%
Test for overall effect: Z = 1.20 (P = 0.23)

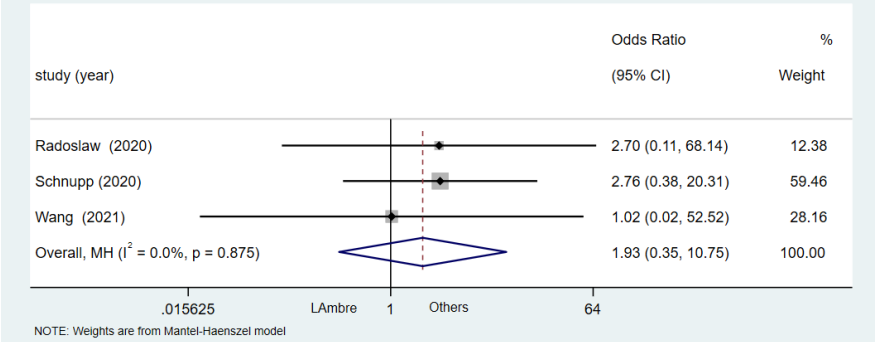


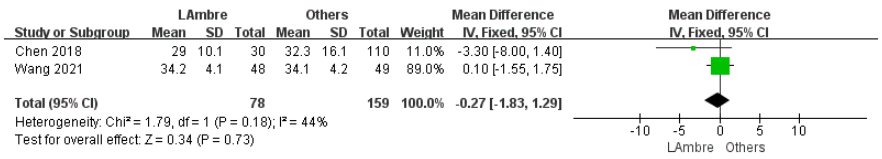
Study or Subgroup	LAmbre Events	LAmbre Total	Others Events	Others Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Chen 2018	30	30	109	110	23.1%	0.84 [0.03, 21.03]
Litwinowicz 2020	24	24	193	199	25.8%	1.65 [0.09, 30.12]
Schnupp 2020	40	40	106	107	21.4%	1.14 [0.05, 28.58]
Wang 2021	47	48	48	49	29.7%	0.98 [0.06, 16.12]
Total (95% CI)		**142**		**465**	**100.0%**	**1.15 [0.26, 5.11]**
Total events	141		456			

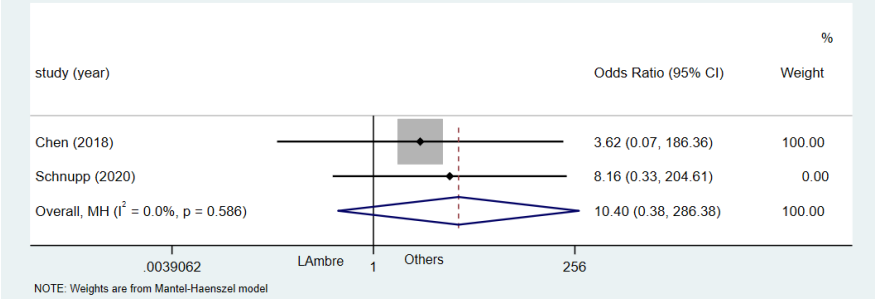
Heterogeneity: Chi² = 0.11, df = 3 (P = 0.99); I² = 0%
Test for overall effect: Z = 0.19 (P = 0.85)

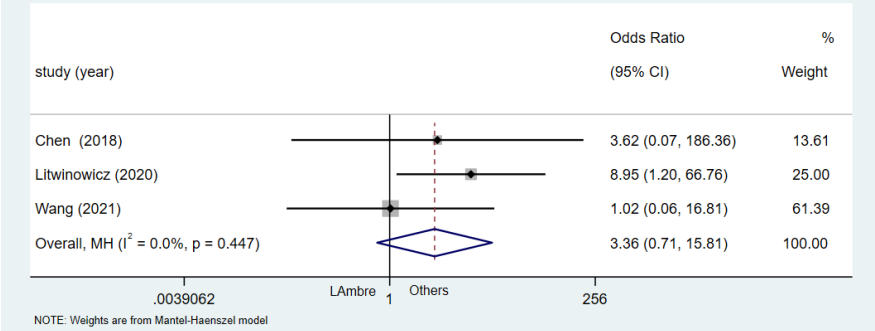


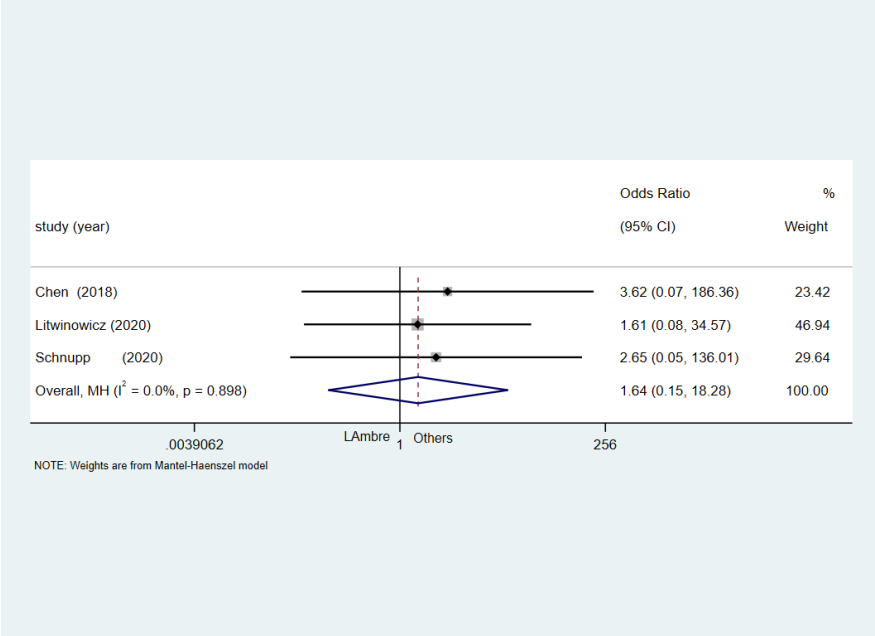


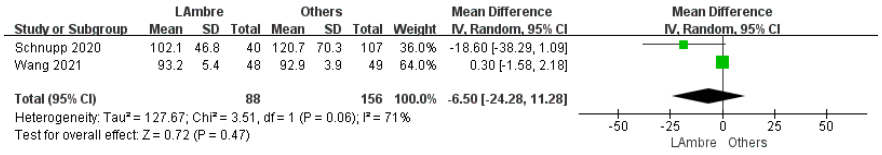












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