MEDwave

Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)
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Is percutaneous closure of the left atrial appendage comparable to anticoagulants for atrial fibrillation?

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Abstract

For most atrial fibrillation patients oral anticoagulation constitutes the standard treatment to prevent stroke. However, they carry a risk of bleeding, which is why alternative treatments have been put into practice, such as percutaneous closure of the left atrial appendage. It is not clear whether this is as effective as the conventional treatment with anticoagulants. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified three systematic reviews including only one pertinent randomized controlled trial. We combined the evidence and generated a summary of findings following the GRADE approach. We concluded that percutaneous left atrial appendage occlusion may decrease stroke and mortality, but the certainty of the evidence is low. The effect on other outcomes is not clear because the certainty of the evidence is very low.

Problem

Stroke is one of the most serious complications of atrial fibrillation. The left atrial appendage is the source of more than 90% of clots in the case of patients with non-valvular atrial fibrillation, which is why the percutaneous closure of the left atrial appendage has become an interesting alternative to the conventional treatment with oral anticoagulants. Despite being a minimally invasive procedure, it may present complications such as severe bleeding and pericardial effusion, among others.

Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages

- Percutaneous left atrial appendage closure compared to anticoagulant treatment may decrease stroke and mortality, but the certainty of the evidence is low.
- The effect on other outcomes is not clear because the certainty of the evidence is very low.
- The probability that future research changes the conclusions presented in this summary is high.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found three systematic reviews [1],[2],[3] including only one randomised controlled trial [4].
What types of patients were included	Mean age of patients was 71 years old, with a CHADS2 score for atrial fibrillation stroke risk of 2.2. None of the patients had contraindication to oral anticoagulation.
What types of interventions were included	This study compared the percutaneous closure of the atrial appendage with warfarin treatment. Patients allocated to the intervention group received percutaneous closure of the left atrial appendage by use of the WATCHMAN device. This device is a self-expanding nickel titanium frame structure with a permeable polyester fabric cover, ranged in diameter from 21 mm to 33 mm. The implantation was guided by flouroscopy and transesophageal echocardiography to verify proper positioning and stability. After the device had been implanted, patients were treated with warfarin for 45 days to facilitate device endothelialization. After stopping warfarin treatment, once daily clopidogrel and aspirin were prescribed until completion of the 6-month follow up visit, from which point aspirin alone was continued indefinitely. For the control group, plasma warfarin concentration was in the therapeutic INR range (between 2.0 and 3.0) 66% of the time.
What types of outcomes were measured	Primary efficacy (ischemic stroke, hemorrhagic stroke, cardiovascular/unexplained death, systemic embolism), any stroke, all-cause mortality. Primary safety: events related to excessive bleeding (i.e. intracranial or gastrointestinal bleeding) or procedure-related complications (i.e. serious pericardial effusion, device embolization, procedure-related stroke). Mean follow-up per patient was 18 months.

Summary of findings

The information on the effects of percutaneous left atrial appendage closure is based on one randomized controlled trial including 707 patients.

- Percutaneous left atrial appendage closure may decrease risk of stroke in comparison to oral anticoagulant treatment. The certainty of the evidence is low.
- Percutaneous left atrial appendage closure may decrease the mortality in comparison with oral anticoagulant treatment. The certainty of the evidence is low.
- It is not clear if percutaneous left atrial appendage closure increases or decreases isquemic stroke in comparison to oral anticoagulant treatment because the certainty of the evidence is very low.
- Percutaneous left atrial appendage closure probably decreases hemorrhagic stroke in comparison to oral anticoagulant treatment. The certainty of the evidence is moderate.
- It is not clear if percutaneous left atrial appendage closure increases or decreases major bleeding because the certainty of the evidence is very low.

Percutaneous left atrial appendage occlusion versus warfarin

Patients Atrial fibrillation
Intervention Percutaneous left atrial appendage occlusion
Comparison Warfarin

Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITH Warfarin	WITH PLAAO		
	Difference: patients per 1000			
Mortality	48 per 1000	30 per 1000	RR 0.62 (0.33 to 1.14)	⊕⊕◯◯ Low[1,2]
	Difference: 18 patients less per 1000 (Margin of error: 32 less to 7 more)			
Any stroke	32 per 1000	23 per 1000	RR 0.71 (0.34 a 1.49)	⊕⊕◯◯ Low[1,2]
	Difference: 9 patients less per 1000 (Margin of error: 21 less to 16 more)			
Ischemic stroke	16 per 1000	22 per 1000	RR 1.34 (0.52 to 3.42)	⊕◯◯◯ Very low[1,2]
	Difference: 5 patients more per 1000 (Margin of error: 8 less to 39 more)			
Haemorrhagic stroke	16 per 1000	1 per 1000	RR 0.09 (0.01 to 0.73)	⊕⊕⊕◯ Moderate[1]
	Difference: 15 patients less per 1000 (Margin of error: 4 to 16 less)			
Major bleeding	41 per 1000	34 per 1000	RR 0.84 (0.39 to 1.83)	⊕◯◯◯ Very low[1,2]
	Difference: 7 patients less per 1000 (Margin of error: 25 less to 34 more)			

RR: Risk ratio.
Margin of error = 95% confidence interval (CI).
GRADE: evidence grades of the GRADE Working Group (see later in this article).

* The risk **WITH WARFARIN** is based on the risk in the control group of the trials. The risk **WITH PLAAO** (and its margin of error) is calculated from relative effect (and its margin of error).

1 We downgraded the certainty of the evidence by one level since the only trial was not blinded.

2 The confidence interval takes into account the possibility of a clinically relevant benefit as well as that of a risk. Because of this, the certainty provided by the evidence related to the outcomes of ischemic stroke and severe bleeding was downgraded in two levels.

About the certainty of the evidence (GRADE)*

⊕⊕⊕⊕
High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕◯
Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕◯◯
Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕◯◯◯
Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.
† Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- This trial only includes patients with paroxysmal non-valvular atrial fibrillation, persistent or permanent, and without contraindication to oral anticoagulation.
- Although it was not directly addressed in the trial, it is reasonable to apply this evidence to patients with contraindication to oral anticoagulation.

About the outcomes included in this summary

- The outcomes presented in this summary are those considered critical for decision-making by the authors of this summary. They are also the ones mentioned in the main clinical guidelines.

Balance between benefits and risks, and certainty of the evidence

- It is currently not possible to carry out a risk/benefit assessment of the procedure, given the certainty provided by the evidence is low. However, it probably decreases hemorrhagic strokes compared with anticoagulant treatment with a moderate level of certainty.
- The percutaneous left atrial appendage closure presents risks during the procedure such as pericardial effusion, severe bleeding, intraprocedural ischemic cerebral stroke and air embolism of the device, which must be weighed against the still uncertain benefits for the medical decision making.

Resource considerations

- The percutaneous closure of the left atrial appendage is an expensive procedure which is also not widely available. In addition, there is little experience in its execution in many centres, which increases the risk of complications.
- Were its effect on mortality certain, the procedure could become cost-effective.

Differences between this summary and other sources

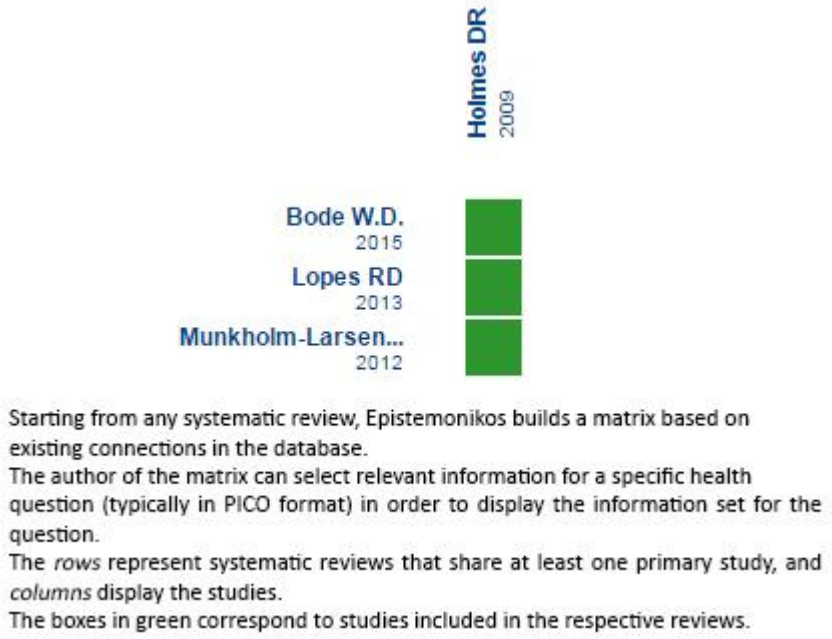
- The conclusions presented in this summary agree with the identified systematic reviews.
- The conclusions of this summary agree with those of the main atrial fibrillation treatment guidelines [5],[6],[7],although with some differences; they consider that there is no evidence confirming the superiority of this procedure to chronic oral anticoagulation yet, but that it is an alternative to oral anticoagulants for patients with a high risk of cerebral stroke with contraindication to chronic oral anticoagulation treatment.

Could this evidence change in the future?

- The likelihood that this information could change in the future is high, due to the low certainty of current evidence.
- There is at least one ongoing study, which has not yielded long term results yet, but will contribute relevant information on this matter [8]. On the other hand, it has been reported a longer term follow-up of the randomized study included in this summary, which is not yet included in existing systematic reviews [9].
- Finally, data from subsequent studies conducted with WATCHMAN devices suggest a mitigation of complications related to the device's implantation, due to the greater experience of surgeons [10].

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.
The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.
The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.
The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version:** Percutaneous atrial appendage occlusion versus warfarin for atrial fibrillation

Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here http://dx.doi.org/10.5867/medwave.2014.06.5997.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

These summaries follow a rigorous process of internal peer review.

Conflicts of interest
The authors do not have relevant interests to declare.

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