Non-contrast computed tomography for the diagnosis of non-traumatic subarachnoid hemorrhage

Yerko Suazo[a,b], Gabriel Rada[b,c,d,e,f]

[a] Facultad de Medicina, Universidad de Chile, Santiago, Chile
[b] Proyecto Epistemonikos, Santiago, Chile
[c] Centro Evidencia UC, Pontificia Universidad Católica de Chile
[d] Departamento de Medicina Interna, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile
[e] The Cochrane Collaboration
[f] GRADE working group

***Corresponding author** radagabriel@epistemonikos.org

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Abstract

Introduction

Subarachnoid hemorrhage is a neurosurgical emergency that requires timely diagnosis due to its severity and the existence of therapeutic measures that are effective when carried out in time. The most used diagnostic sequence to rule it out is computed tomography without contrast which, if negative, is followed by lumbar puncture. However, it has been suggested that a negative non-contrast computed tomography (without blood) may rule out the diagnosis.

Methods

To answer this question we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach.

Results and conclusions

We identified three systematic reviews including nine studies. We concluded the diagnostic accuracy of non-contrast computed tomography is probably very high, but the clinical impact of relying only on this test has not yet been evaluated.

Problem

It is estimated that subarachnoid hemorrhage could be responsible for 1% of headaches in emergency services[1,2]. Its early diagnosis is very important since it is a neurosurgical emergency with very high morbidity and mortality, and there are therapies that can make an important difference if timely implemented[2]. Although it has a characteristic clinical presentation, the symptoms and signs are not enough to rule it out[1,2]. The most commonly used sequence is non-contrast computed tomography followed by a lumbar

puncture, ruling out the condition with both results negative. However, lumbar puncture is not risk-free (infection, hematoma, and stress for the patient) and its added value is a matter of debate[1,2].

Key messages

- Diagnostic accuracy of non-contrast computed tomography for non-traumatic subarachnoid hemorrhage is probably very high, although its clinical impact has not yet been evaluated.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found three systematic reviews[1-3] that included nine primary studies overall[4-12], none of them a randomized trial. We did not find studies evaluating the clinical impact. We excluded one systematic review[3] because it mixed non-traumatic with peri-mesencephalic subarachnoid hemorrhage, which is considered a different clinical entity.
What types of patients were included*	All studies included patients older than 11 years, four studies included adults without specifying age[5,6,9,12] and four studies only included patients without neurological deficit[5,7,11,12]. Five studies evaluated patients with less than 6 hours symptom onset[6,7,9,11,12], one study with less than 12 hour[5] and three studies did not specify it[4,8,10]. One study[6] only included patients with negative non-contrast computed tomography for subarachnoid hemorrhage.
What types of interventions were included*	Five studies used 16-slice or higher computed tomography[6,7,9,11,12] and the others did not described the type of computed tomography used[4,5,8,10]. As gold standard, six studies used lumbar puncture, imaging, and follow-up[6,7,8,9,11,12] and the rest did not reported it[4,5,10]. Five studies followed all of their patients[6-9,11], three studies did not follow up patients[4,5,10] and one study had an incomplete follow up (86% of patients)[12].
What types of outcomes were measured	The different systematic reviews pooled outcomes as follows: specificity, sensitivity, positive likelihood ratio (LR +), negative likelihood ratio (LR -), true positives, false negatives, false positives and true negatives.

* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

Methods

To answer the question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and reanalyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) 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 when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Summary of Findings

Information on the diagnostic accuracy of non-contrast computed tomography for non-traumatic subarachnoid hemorrhage is based on 9 primary studies[5-13]. All of these measured specificity, sensitivity, LR + and LR- of the non-contrast computed tomography for non-traumatic subarachnoid hemorrhage.

The summary of the findings is as follows:

- It is not clear if non-contrast computed tomography for non-traumatic subarachnoid hemorrhage impacts mortality and morbidity because we did not find studies evaluating this aspect
- Diagnostic accuracy of non-contrast computed tomography for non-traumatic subarachnoid hemorrhage is probably very high.

Non-contrast computed tomography in suspicion of subarachnoid hemorrhage			
Patients	Suspected subarachnoid hemorrhage, with less than 6 hours of symptoms, without neurological deficit		
Intervention	Non-contrast computed tomography		
Comparison	Computerized tomography, lumbar puncture and clinical follow-up		
Diagnostic Impact			
Outcomes	Effect		
Morbidity or mortality	We did not identify studies assessing the diagnostic impact, so the outcome was estimated from diagnostic accuracy and the expected consequences from each result.		
Diagnostic accuracy			
Outcome	Effect for 10000 tested patients (CI 95%)	Certainty of the evidence (GRADE)**	Hypothetical clinical impact
Sensitivity: 98.7% (CI 95% from 97.1 to 99.4 %) Specificity: 99.9 % (CI 95% from 99.3 to 100%) LR (+): 921.9 (IC 95% from 139 to 6103) LR (-): 0.010 (IC 95% from 0.003 to 0.034) Hypothetical prevalence 1%* (100 patients with and 9900 without the condition)			
Positive screening, correct diagnosis of non-traumatic subarachnoid hemorrhage (true positives)	99	⊕⊕⊕◯[1] Moderate	The test correctly diagnoses 99 out of 100 patients with non-traumatic subarachnoid hemorrhage.
Negative screening, correct discard of non-traumatic subarachnoid hemorrhage (true negatives)	9890	⊕⊕⊕◯[1] Moderate	The test rules out the condition in 9890 out of 9900 patients who do not present non-traumatic subarachnoid hemorrhage, avoiding risky procedures (mainly lumbar puncture).
Positive screening, incorrect diagnosis of non-traumatic subarachnoid hemorrhage (false positives)	10	⊕⊕⊕◯[1] Moderate	Computed tomography without contrast incorrectly diagnoses 10 out of 9900 patients without the condition, leading to risky procedures (mainly lumbar puncture).
Negative screening, incorrect discard of non-traumatic subarachnoid hemorrhage (false negatives)	1	⊕⊕⊕◯[1] Moderate	One out of 100 patients with the condition is not detected by non-contrast computed tomography, which could lead to late diagnosis, poor prognosis and even death.
CI: Confidence interval (95%) GRADE: evidence grade, from GRADE Working Group *The prevalence corresponds to acute headaches episodes that consult the emergency service **Diagnostic accuracy [1] The certainty of evidence was downgraded in one level due to the risk of bias, since studies had selection bias and incomplete follow-up.			

Follow the link to access the interactive version of this table (Interactive Summary of Findings – iSoF)

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.

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* 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

The evidence analyzed in this summary applies to adults without neurological deficit, with early onset of symptoms (less than 6 hours), that consult to emergency services for intense headache, evaluated by a radiologist, with a modern computed tomography.

This evidence should be applied cautiously to children, adolescents and especially to patients with neurological deficit, since these groups are not well represented in the studies.

About the outcomes included in this summary

We conducted searches on the diagnostic impact of non-contrast computed tomography, but no systematic reviews that answered this question were found. So, the search was expanded in order to find systematic reviews on diagnostic accuracy, which reported sensitivity, specificity and likelihood ratios.

Balance between benefits and risks, and certainty of the evidence

Because of the lack of systematic reviews addressing diagnostic impact, It is difficult to make a balance between risk and benefits. However, based on the good diagnostic accuracy, it is reasonable to anticipate a balance in favour of non contrast computed tomography. On the other hand, adverse effects are only those derived from radiation and from the decisions associated to false positives and false negatives (false security or unnecessary actions).

Resource considerations

Reducing the need to perform contrasted exams or lumbar puncture could lead to savings, particularly in scenarios where carrying out this procedure requires unavailable resources or transfer to other centers.

What would patients and their doctors think about this intervention

With the information presented in this summary, most clinicians should lean in favor of simply relying on non contrast computed tomography.

However, due to the lack of evidence on diagnostic impact in clinical practice, the decision making in this area will probably vary.

Differences between this summary and other sources

The systematic reviews identified agree with this summary in terms of the accuracy of computed tomography in this setting, and the lack of benefit of performing a subsequent lumbar puncture. On the other hand they conclude computed tomography and lumbar puncture, or even angiography, may be necessary in patients with symptoms for more than 6 hours.

The guideline of the American Heart Association /American Stroke Association recommends performing lumbar puncture whenever there is suspicion of subarachnoid hemorrhage with negative computed tomography[14]. The European guideline recommends performing lumbar puncture after early negative computed tomography only if there is high clinical suspicion of subarachnoid hemorrhage[15].

Could this evidence change in the future?

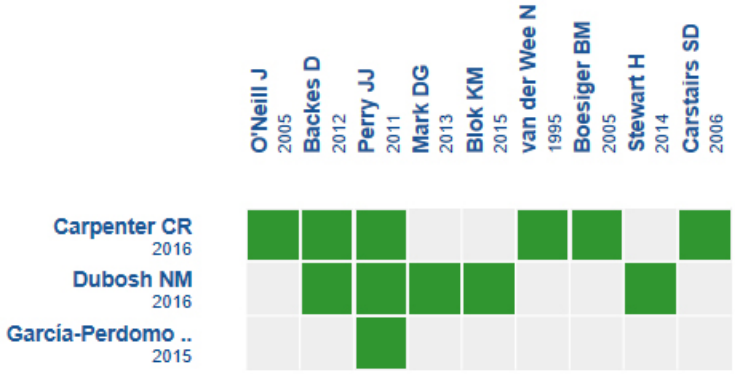
The probability that future research changes the conclusions of this summary for diagnostic impact is high, due to the uncertainty of the existing evidence, and low for diagnostic accuracy.

The American Heart Association presents one study in its clinical guideline that is not included in any systematic review[16], where patients are separated in terms of days of evolution, not in hours. New reviews incoporating this variable might be of value.

We identified one ongoing systematic review of cost-benefit in PROSPERO[17], and one observational study in the Clinical Trials Registry Platform of the World Health Organization[18].

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.



An evidence matrix is a table that compares systematic reviews that answer the same question.
Rows represent systematic reviews, and columns show primary studies.
The boxes in green correspond to studies included in the respective revisions.
The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version:** Accuracy of computed tomography without contrast for the diagnosis of non-traumatic subarachnoid hemorrhage

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.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE 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.

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Correspondencia a
Centro Evidencia UC
Pontificia Universidad Católica de Chile
Diagonal Paraguay 476
Santiago
Chile