Reviewer's report

Title: A prediction rule for acute adverse reactions from contrast agents for computed tomography

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Reviewer: Ingrid Böhm

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A prediction rule for acute adverse reactions from contrast agents for computed tomography

Reviewers' general comments

The authors retrospectively analyzed 36,472 patients who underwent enhanced CT imaging during a period of seven years. They found 756 patients (2%) with adverse reactions. By using logistic regression analysis they revealed that prior adverse reaction to contrast agents, urticaria, an allergic history to drugs other than contrast agents, contrast agent concentration >70%, age <50 years, and total contrast agent dose >65 g were significant predictors for an acute adverse reaction. Thereby, the authors confirmed previous studies dealing with adverse reactions induced by contrast agents. The goal of the study is unclear, because on one hand the authors focus on the "pre- and post-imaging management of patients" and on the other hand they intended "to predict the incidence of acute adverse reactions to contrast agents". Moreover, the definition of investigated adverse reactions is unclear: all adverse reactions or hypersensitivity reactions (the latter can be subdivided in allergic and non-allergic reactions)?

Reviewers' specific comments

Title

The title suggests that the authors will give some practical hints to predict adverse reactions, but the paper does not provide this. Therefore, it would be better to use another title.
Abstract

Introduction

"In Japan, the number of CT scans performed is not only substantially higher than in other countries, but continues to increase". Please provide the number of CT scans performed in Japan. The second part of the sentence should be deleted, because in other countries the number of CT scans continues also to increase (Katzberg RW. "Acute reactions to urographic contrast medium: incidence, clinical characteristics, and relationship to history of hypersensitivity states"--a commentary. AJR Am J Roentgenol. 2008 Jun;190(6):1431-2).

"Symptoms of an adverse reaction to contrast agents are diverse ranging from flushing, pruritus, urticaria, and angioedema, with more severe side effects including hypotension, loss of consciousness, to potentially life-threatening bronchospasm and airway obstruction".

The mentioned symptoms are all hypersensitivity reactions that may be either allergic or non-allergic (Böhm I et al. Contrast-media-induced hypersensitivity or allergic/allergic-like reactions? Suggestion for a more appropriate use of the nomenclature. Eur J Clin Pharmacol. 2008 Sep;64(9):931-2). Please correct this. Furthermore, please explain in detail which adverse reaction (see above) you’d like to investigate.

"A prediction rule may facilitate the pre- and post-imaging management of patients requiring contrast enhanced CT imaging." Please explain in form of an example (3-5 cases) how it should work in clinical routine practice.

"The goal of this study is to predict the incidence of acute adverse reactions to contrast agents based on relevant patient demographic and clinical factors." Please re-write this sentence, because your study is not able to predict the incidence of acute adverse reactions to contrast media.

Methods

How many physicians/radiologists examined the patients?

Please provide a checklist (in form of a table) with all parameters you retrospectively analyzed.
Acute adverse reactions to contrast agents, defined per anaphylaxis criteria as occurring at or within 24 hours. This definition (Ellis AK, Day JH. Diagnosis and management of anaphylaxis. CMAJ 2003;169:307-11) is based on a 19-year-old woman with a history of seasonal allergic rhinitis who reacted to an injection of an allergen immunotherapy. For patients with contrast media induced adverse reactions it is inappropriate. Please use the definition of most studies (e.g. Schild HH et al. Adverse events after unenhanced and monomeric and dimeric contrast-enhanced CT: a prospective randomized controlled trial. Radiology. 2006 Jul;240(1):56-64) that deal with contrast media induced adverse reactions:

- Acute reactions occur immediately during the injection of the contrast agents up to one hour afterwards.
- Non-acute (delayed) reactions occur more than one hour after the injection of the contrast agent.

How did you allocate patients to the derivation group or validation group? In your abstract you mention that you randomly divided the patients. I do not understand why you built this two groups. To my opinion it would be much more interesting to compare reactors and non-reactors.

A definition of the severity of the reactions is missing. Please provide this (Böhm I et al. Eur J Radiol. 2011 Nov;80(2):368-72).

Results

Why did you provide the tables as additional files? Please insert the tables in your manuscript.

"Severe reactions, such as shock, #" as mentioned above you should insert a definition of the severity grades. Comparing two randomly formed groups is not very exciting (as mentioned above).

"The most frequent reaction was nausea and/or vomiting at 241 occurrences #" Isolated occurring nausea and vomiting are common adverse reactions, in the context
with other symptoms such as urticaria, angioedema etc. They can be by hypersensitivity reactions.

Therefore, it is important that you clearly state which kind of adverse reaction you like to analyze: common adverse reactions or hypersensitivity reactions (see above).

"All patients were prescribed non-ionic, low-osmolar contrast agents (iopamidol, iohexol, ioversol or iomeprol)." It would be interesting to show in detail how many reactors received the above listed contrast media, and how many non-reactors. Do the percentages differ between these two groups?

Discussion

"In this study, we propose a prediction model for estimating the incidence of acute adverse reaction in patients undergoing contrast enhanced CT imaging." What does this mean? Do you like to provide a model for the management of single patients before they receive the contrast material or do you like to present a mathematical model for the estimation of the incidence of reactions?

You should clearly state what you like to present. Therefore, it is necessary (as mentioned above) that you exactly define what kind of adverse reaction you like to analyze.

Conclusion

The listed risks are well known. Therefore, it would be helpful to show in single (e.g. five patients) cases how your prediction rule works. Moreover, it is unclear which practical consequences will follow.

References

3/26 refs are older than six years. It is recommended to cite more recent published papers.

Figure 1

I do not understand this figure. What does '0-2', '3-5', '6-8' and '9-' mean? Please explain this in the legend.