

University of Groningen

Response to Chen et al

Klompenhouwer, Anne J; Alblas, Maaïke; van Rosmalen, Belle V; Haring, Martijn P D; Venema, Esmee; Doukas, Michael; Thomeer, Maarten G J; Takkenberg, Robert B; Verheij, Joanne; de Meijer, Vincent E

Published in:
AMERICAN JOURNAL OF GASTROENTEROLOGY

DOI:
[10.14309/ajg.000000000000488](https://doi.org/10.14309/ajg.000000000000488)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Klompenhouwer, A. J., Alblas, M., van Rosmalen, B. V., Haring, M. P. D., Venema, E., Doukas, M., Thomeer, M. G. J., Takkenberg, R. B., Verheij, J., de Meijer, V. E., van Gulik, T. M., Lingsma, H. F., de Man, R. A., & Ijzermans, J. N. M. (2020). Response to Chen et al: More Information Needed Response. *AMERICAN JOURNAL OF GASTROENTEROLOGY*, 115(1), 147-148. <https://doi.org/10.14309/ajg.000000000000488>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

adenoma (HCA), estimating the probability of HCA regression to <5 cm at 1 and 2 years of follow-up. The results showed that the C-statistic of overall predictive ability for regression to <5 cm was 0.79 (95% confidence interval: 0.73–0.85) by internal validation. HCA is a rare, benign liver tumor. Although the prediction model still requires external validation in an independent study population, we still believe this model can help clinicians in decision making and avoid unnecessary surgery. However, we also would like to highlight a few important issues regarding this article.

First, when the model used for decision making of surgery for large size of HCA, we think decision curve analysis (DCA) should be used along with the receiver operating characteristic (ROC) curve. DCA is a method for evaluating the benefits of a prediction model across a range of patient preferences for accepting the risk of undertreatment and overtreatment to facilitate decisions about test selection and use (2). The ROC metric focuses solely on the predictive accuracy of a model. A model that had a much greater specificity but slightly lower sensitivity than another would have a higher AUC but would be a poorer choice for clinical use (2). DCA has been recommended by *JAMA* (3), *BMJ* (4), and several other major journals. We think the DCA should be used for evaluating the net benefits when decision making of surgery based on this model and comparing the net benefits when decision making by HCA not regress to <5 cm after 6 or 12 months.

Second, the authors measured the discrimination power of the prediction model with C-statistic. Discrimination power is the ability of the model to correctly separate the subjects into different groups. But we think a prediction model should be tested by its discrimination power and calibration power. Calibration power is the degree of correspondence between the estimated probability produced by the model and the actual observed probability (5). Common assessments used in calibration for confidence of fit include misclassification rate, Pearson's χ^2 , interrater agreement with kappa value, or Hosmer-Lemeshow statistic. The calibration curve was constructed by correlating the predicted incidence with the actual incidences within either score in the model. From the assessment tool (available via <https://hcaprediction.shinyapps.io/calculator/>) provided by the authors, we can calculate predicted incidence of regression to <5 cm of 1 year and after diagnosis. But we

cannot find the actual incidences of regression to <5 cm of 1 year and after diagnosis. We want to know the Hosmer-Lemeshow statistic of calibration power for the model predicting regression of large-size HCA, and we also want to see the calibration curves with predicted incidence and actual incidences.

In summary, the authors developed a prediction model, estimating the probability of HCA regression to <5 cm at 1 and 2 years of follow-up, and the model can be useful in helping clinicians in decision making and avoid unnecessary surgery. However, we think the DCA and calibration power analysis should be used before clinical decision.

CONFLICTS OF INTEREST

Guarantor of the article: Kun Liu, MD.

Specific author contributions: H.-L.C., Y.-P.S., and K.L. wrote the letter.

Financial support: None.

Potential competing interests: None.

REFERENCES

1. Klompenhouwer AJ, Alblas M, Vivica van Rosmalen B, et al. Development and validation of a model to predict regression of large size hepatocellular adenoma. *Am J Gastroenterol* 2019;114:1292–8.
2. Vickers AJ, Elkin EB. Decision curve analysis: A novel method for evaluating prediction models. *Med Decis Making* 2006;26:565–74.
3. Fitzgerald M, Saville BR, Lewis RJ. Decision curve analysis. *JAMA* 2015;313:409–10.
4. Vickers AJ, Van Calster B, Steyerberg EW. Net benefit approaches to the evaluation of prediction models, molecular markers, and diagnostic tests. *BMJ* 2016;352:i6.
5. Chiu JS, Yu FC, Li YC. Discrimination and calibration are concurrently required for model comparison. *Int J Cardiol* 2006;112:245–6.

¹School of Public Health, Nantong University, Nantong City, Jiangsu Province, China P.R.

²School of Medicine, Nantong University, Nantong City, Jiangsu Province, China P.R.; ³Department of Surgery, Hospital of Nantong University, Nantong City, Jiangsu Province, China P.R.

Correspondence: Kun Liu, MD.
E-mail: jsntliukun@sina.com.

Response to Chen et al

Anne J. Klompenhouwer, MD, PhD¹,
Maaïke Alblas, MSc²,
Belle V. van Rosmalen, BSc³,
Martijn P.D. Haring, MD⁴,
Esmee Venema, MSc, PhD²,

Michael Doukas, MD, PhD⁵,
Maarten G.J. Thomeer, MD, PhD⁶,
Robert B. Takkenberg, MD, PhD⁷,
Joanne Verheij, MD, PhD⁸,
Vincent E. de Meijer, MD, PhD⁴,
Thomas M. van Gulik, MD, PhD³,
Hester F. Lingsma, MSc, PhD²,
Robert A. de Man, MD, PhD⁹ and
Jan N.M. Ijzermans, MD, PhD¹

Am J Gastroenterol 2020;115:147–148. <https://doi.org/10.14309/ajg.000000000000488>

We thank Chen et al. (1) for taking an interest in our article, and we address the issues raised.

Their first point regarding the decision curve analysis (DCA) is indeed very interesting. In DCA, consequences of different treatment strategies are incorporated and are used to evaluate whether a model is worth using (2). A DCA requires a binary decision: surgery vs wait-and-see in our case. Next, we should consider a weight to put on false-positive vs false-negative decisions. In other words, how many patients would we be willing to operate, although they will regress to avoid one patient not regressing while treated conservatively. This would entail having detailed information on surgical complications but also on malignant transformation and hemorrhage in those who are treated conservatively. In the study population used for model development, no hemorrhage or malignant transformation occurred. To perform a DCA, a larger population is needed providing a better estimation of the risks and benefits of the different treatment strategies.

We tend to disagree with Chen et al. (1) on their second point regarding the calibration of the model. As they point out, calibration power is the degree of correspondence between the estimated probability produced by a model and the actual observed probability. As this model was only internally validated, the calibration is always perfect. Only in a model that is externally validated, calibration analysis provides additional information, and calibration plots should be performed.

CONFLICTS OF INTEREST

Guarantor of the article: Anne Julia Klompenhouwer, MD, PhD.

Specific author contributions: None to report.

Financial support: None to report.

Potential competing interests: None to report.

REFERENCES

1. Chen HL, Song YP, Liu K. Model to predict regression of large-size hepatocellular adenoma: More information needed. *Am J Gastroenterol* 2020;115:146–7.
2. Vickers AJ, Elkin EB. Decision curve analysis: A novel method for evaluating prediction models. *Med Decis Making* 2006;26:565–74.

¹Department of Surgery, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands; ²Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the

Netherlands; ³Department of Surgery, Amsterdam University Medical Centers, University of Amsterdam (Location Academic Medical Center), Amsterdam, the Netherlands; ⁴Division of Hepatopancreatobiliary Surgery and Liver Transplantation, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands; ⁵Department of Pathology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands; ⁶Department of Radiology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands;

⁷Department of Gastroenterology and Hepatology, Amsterdam University Medical Centers, University of Amsterdam (Location Academic Medical Center), Amsterdam, the Netherlands; ⁸Department of Pathology, Amsterdam University Medical Centers, University of Amsterdam (Location Academic Medical Center), Amsterdam, the Netherlands; ⁹Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands.

Correspondence: J.N.M. IJzermans, MD, PhD.
E-mail: j.ijzermans@erasmusmc.nl.