Author’s response to reviews

**Title:** Comparison of the Prognostic Values of Three Calculation Methods for Echocardiographic Relative Wall Thickness in Acute Decompensated Heart Failure: A Retrospective Study

**Authors:**

Satoshi Yamaguchi (satoshi-yamaguchi@umin.ac.jp)

Michio Shimabukuro (mshimabukuro-ur@umin.ac.jp)

Masami Abe (mabe@yuuai.or.jp)

Tomohiro Arakaki (tarakaki@yuuai.or.jp)

Osamu Arasaki (oarasaki@yuuai.or.jp)

Shinichiro Ueda (blessyou@med.u-ryukyu.ac.jp)

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Point by point

Reviewer #1: This is an interesting study about prognostic significance of a relatively simple echocardiographic parameter like RWT but there are some critical issues that need to be addressed. (Response) Thank you for your positive comments on our manuscript. Low RWT groups have significantly lower EF, higher LVEDV, higher prevalence of severe MR, higher (numerically) pro-BNP, all known negative prognostic factors. Paradoxically they have less mortality. Was this population affected by HFpEF? Please the authors comment and try to explain the reason in the discussion. (Response) Thank you for your comments on the important points. We found that our study population included 157/383 (41%) HFpEF patients (LVEF ≥ 50%; revised Table 1). (Page 7, Line 16) There were significant positive correlations between the three RWTs and age and LVEF, and negative correlations between the RWTs and LogBNP and LVEDV (Table 4). (Page 10, Line 3) Paradoxically, high-RWTPW patients had lower BNP than low-RWTPW patients (Table 1). High-RWTPW patients included 101 (53%) patients. Generally, BNP increases modestly in HFpEF [18]. Furthermore, the prognostic value of BNP has not been confirmed in patients with HFpEF [19]. High RWTPW might be of clinically utility. (Page 10, Line 8) Patients having valvular diseases with various etiologies were included, which might affect the prognostic value of RWTs. Suggestions: Diastolic blood pressure and hospital stay in days should be reported if available. (Response) Thank you for your suggestions. We show diastolic pressure and hospital stay in Table 1.Grammatical errors: In the abstract line 19: Only adjusted Cox model showed that High-RWTPW should be showed that High-RWTIVS+PWIn the abstract "was a significant risk of the primary outcome". Line 10 page 1 left ventricle wall tickness "is represented by" IVS and PW. Line 19 page 1 "were examined and compared" should be deleted. (Response) Thank you for your careful review. We revised along to your advices.

Reviewer #2: The echocardiographic relative wall thickness is essential in the clinical
arena. It is mainly useful for categorization of an increase in LV mass as either concentric (RWT > 0.42) or eccentric (RWT ≤ 0.42) hypertrophy, and for identification of concentric remodeling (normal LV mass with increased RWT). The relative wall thickness could be assessed using both septal and posterior wall thickness, or just one of these walls thickness. It is interesting to note that the actual Chamber Quantification Guidelines recommend calculating the relative wall thickness using the formula: 2 (posterior wall thickness)/(LV internal diameter at end-diastole). However, there is no cited reference embasing this recommendation to use only the posterior wall thickness on the formula. Reviewing the literature, we can find papers demonstrating the clinical impact of the relative wall thickness despitied to the used methodology. But none paper performed a comparison among the different formulas. In the present manuscript, the author aimed to fill this scientific gap. They performed a direct comparison among the three different methods for calculating the echocardiographic relative wall thickness concerning the prognostic value. It is a single-center retrospective cohort of 426 consecutive patients admitted due to acute decompensated heart failure in an emergency department between June/2014 to April/2016. From the 426 enrolled patients, just 385 were eligible for the analysis. The primary outcome was all-cause of death, but in some analysis, the authors use hospital admission or mortality as a and 90-day outcome. The paper is interesting and well written. However, there are some points to be reviewed: (Response) Thank you for your understanding of our study aims. We are sorry for the confusing description. The primary outcome was all-cause death throughout our manuscript. Major concerns:- Please review all manuscript using the STARD recommendations check-list (http://www.equator-network.org/reporting-guidelines/stard/) and include as Figure 1 an enrolment flow-chart. (Response) We appreciate your valuable comments on our manuscript. We added Figure 1. We checked throughout our manuscript, using the STARD recommendations. Please see attached check list. - I would suggest to better describe in the methodology section, which was the primary and secondary outcomes. There are results presented in a 90-day follow-up, which I guess also considered admission and not just death. Also, it is essential to explain how the follow-up was assessed and cite how many patients were lost during the follow-up period. The Kaplan-Meier graphs display a longer than 600 days follow-up. How long were the average follow-up and the interquartile interval? (Response) Thank you very much for your important comments. Cardiologists followed-up the patients at the clinic. (Page 3, Line 2) Cardiologists followed the patients at Tomishiro Central Hospital Clinic every 1-3 months after hospital discharge. Medical clerks confirmed the patients’ condition if the patients canceled the appointment. (Page 3, Line 25) A total of 48 patients who were lost to follow-up were excluded to evaluate the risk of 90-day mortality. We shows the median [25%, 75%] of the followed-up days in survival analysis and logistic regression analysis. (Page 3, Line 19) During follow-up (235 [92, 425] days), 95 (25%) patients died. - Why the authors used the mean value of the relative wall thickness as a cut-off to divide the respective method groups? Why not use the cut-off provided on the Chamber Quantification Guidelines or the cut-off derived from the respective ROC curve (c-statistic)? I guess it could change the results. (Response) Thank you for your comments. To make sure of the tendency, we used the median of the RWTs. We obtained the best cut-off for the 90 days mortality. Therefore, we added the survival analysis with the cut-off of the best cut-off for 90 days mortality. We confirmed that the consistency with the result of main analysis (Figure S1, Table S2). - The authors tested the reliability of the measurement of PWth and IVSth in an offline way. However, there is no description in the methodology section if these echo studies were storage or not. Please review it. (Response) Thank you very much. The TTE image had been stored in the local server and medical technician and two other examiners re-measures in the TTE image