Jugular venous ultrasound predicts outcomes in pulmonary hypertension outpatients

To the Editor:

Assessment of jugular venous pressure (JVP) is a classic physical examination manoeuvre that serves as an estimate of right atrial pressure (RAP). Although JVP was rated by experts as the most important physical examination finding to monitor response to therapy in pulmonary hypertension (PH) patients [1], it has been understudied in PH. Since RAP is an accurate predictor of outcome in PH [2, 3], determining whether clinically assessed JVP (as a non-invasive surrogate for RAP) also predicts outcomes is an important, unanswered question. Since JVP can be difficult to measure on physical examination due to obesity and challenges distinguishing between carotid and jugular pulsations, ultrasound measures of JVP have been developed [4, 5]. We hypothesised that: 1) JVP measurement could be more reliably obtained by ultrasound (JVP-US) than JVP by physical examination (JVP-exam); 2) JVP-US would correlate with same-day B-type natriuretic peptide (BNP), another non-invasive surrogate of right heart function; and 3) JVP-US would predict time to clinical worsening (TTCW).

This was a prospective, observational study at a United States Pulmonary Hypertension Association-accredited Comprehensive Care Center enrolling patients from July 2016 to April 2018, with follow-up ending April 2021. Consecutive patients from any World Symposium on Pulmonary Hypertension (WSPH) subgroup [6] were eligible for inclusion. Informed consent was obtained from each patient prior to enrolment (IRB #9403, clinicaltrials.gov NCT02873039).

The REVEAL 2.0 risk score [2], a multi-parameter risk prediction score, was calculated using the most recent data from the medical record. The research team was blinded to patient's clinical status and BNP, and the treating physician was blinded to the results of the ultrasound measurement. A physical examination estimate of JVP ("JVP-exam") was performed by the treating physician by adding 5 cmH$_2$O to the measured vertical height of the right internal jugular vein (IJV) V-wave above the sternal angle with the patient seated at a 45-degree angle. A handheld ultrasound device (General Electric Vscan) was used to estimate JVP in the right IJV [4] with the patient in the same position. The probe was placed in a horizontal position in the anterior triangle of the neck and then rotated 90 degrees to obtain a longitudinal view of the jugular vein. The vertical height of the IJV tapering above the sternal angle clavicle plus 5 cmH$_2$O was used to estimate JVP ("JVP-US") (figure 1a). JVP measurements were taken at end-expiration.

Baseline descriptive statistics were calculated and reported as mean±SD or percentages. Bland–Altman analysis was conducted to compare JVP-exam to JVP-US. Pearson correlation coefficients were calculated for both JVP-exam and JVP-US in relation to log-transformed BNP. Participants were followed prospectively for their first clinical worsening event (first occurrence of death, lung transplantation, PH-related hospitalisation, or worsening functional class (FC) with addition of PH-specific medication [7]). Cox regression analysis was conducted to assess the relationship between JVP-exam and JVP-US and TTCW, with adjustment for REVEAL 2.0 risk score. There was no significant collinearity between JVP measurements and REVEAL 2.0 risk score, based on a variable inflation factor <10.

90 PH patients were included, with the majority having pulmonary arterial hypertension or chronic thromboembolic PH (61% and 13%, respectively); 60% of patients were on PH-specific medications at

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Jugular venous pressure estimated using a handheld ultrasound device was able to predict clinical worsening in pulmonary hypertension outpatients, even after adjusting for REVEAL risk score https://bit.ly/3nNnKZ8
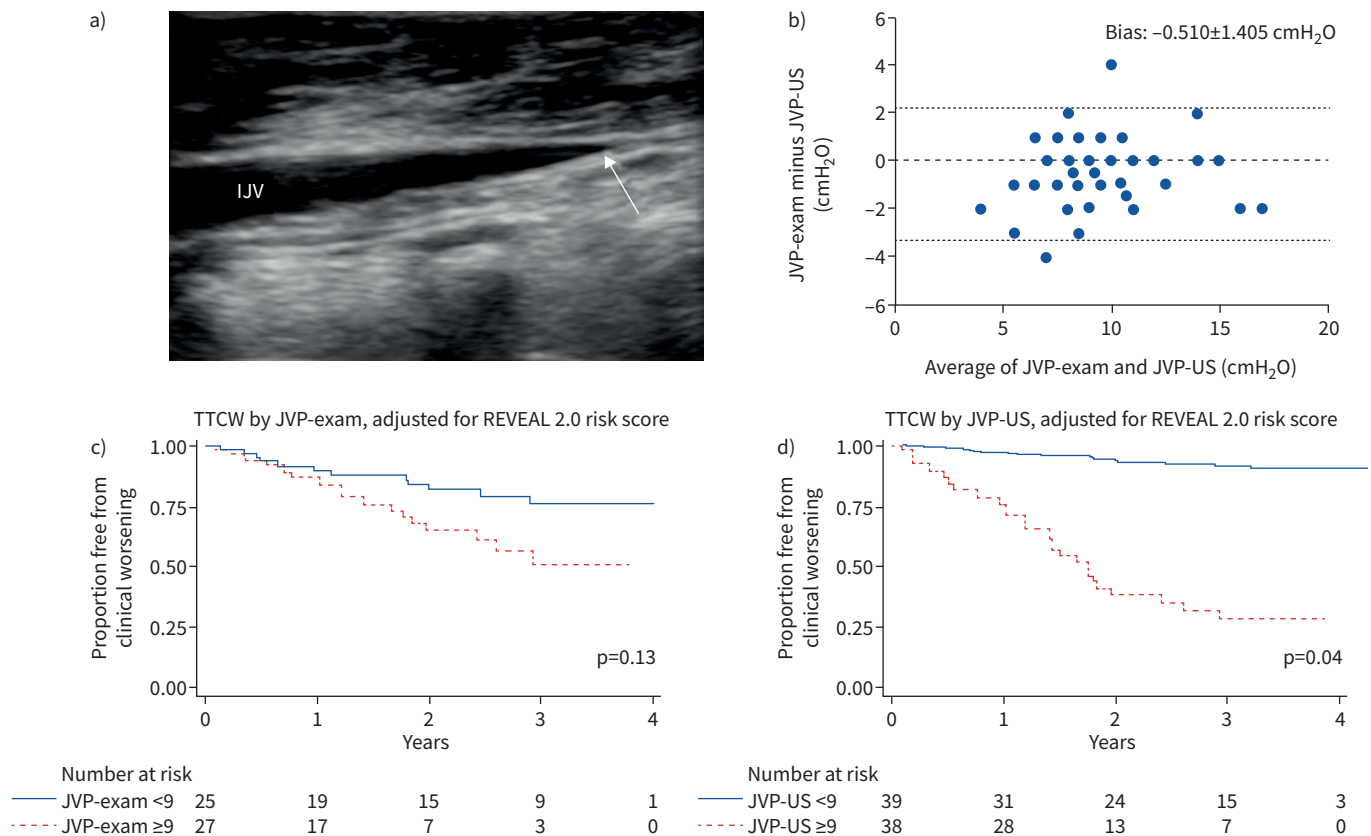
FIGURE 1 a) Ultrasound image of the internal jugular vein (IJV) in the longitudinal view. The point of tapering (arrow) was determined and jugular venous pressure (JVP) was derived as outlined in the main text. b) Bland–Altman plot showing the agreement between JVP by physical examination (JVP-exam) and ultrasound (JVP-US) (n=50 patients with both JVP-exam and JVP-US possible; some data points are superimposed). Dotted lines are the 95% limits of agreement. c and d) Kaplan–Meier curves for time to clinical worsening (TTCW) by median JVP by c) physical examination and d) ultrasound, both adjusted for REVEAL 2.0 risk score.

study enrolment. The majority were FC II (55%) or III (38%) and the average REVEAL 2.0 risk score was 7±3; the median number of parameters available for each patient to calculate the REVEAL 2.0 score was 11.5, out of a possible 13 variables in the calculator. Full baseline characteristics of this cohort have been previously described [8].

JVP-exam was feasible in only 60% of patients. In contrast, JVP-US was measurable in 88% of patients ($p < 0.0001$ compared to JVP-exam) in a median time of 1 min (interquartile range 1–2 min). The average difference between JVP-exam and JVP-US was -0.5 ± 1.4 cmH$_2$O (95% limits of agreement −3.3 to 2.2). JVP-exam moderately correlated to logBNP (r=0.60, $p < 0.0001$, n=48), although JVP-US only weakly correlated with logBNP (r=0.39, p=0.001, n=69).

49 participants experienced at least one clinical worsening event (death, n=12; transplant, n=2; hospitalisation, n=26; worsened FC with medication added, n=9) for a median at-risk follow-up of 2 years (interquartile range 1–3). JVP-exam (HR 1.12, 95% CI 1.01–1.26; p=0.03) and JVP-US (HR 1.18, 95% CI 1.05–1.32; p=0.004) were both associated with TTCW. When adjusted for REVEAL 2.0 risk score, JVP-exam was no longer associated with TTCW (HR 1.09, 95% CI 0.97–1.23; p=0.13) (figure 1c); however, JVP-US was independently associated with TTCW after adjustment for REVEAL 2.0 risk score (HR 1.13, 95% CI 1.00–1.27; p=0.04) (figure 1d). In a sensitivity analysis restricted to WSPH group 1 and 4 patients, the results were similar (JVP-exam, after adjusting for REVEAL 2.0: HR 1.11, 95% CI 0.97–1.27, p=0.12; and JVP-US, after adjusting for REVEAL 2.0: HR 1.18, 95% CI 1.02–1.36, p=0.02).

In this prospective, observational study, we found that ultrasound measures of JVP were quick and highly feasible in the outpatient setting, and were independently associated with clinically important outcomes. To

our knowledge, this is the first study to investigate the association of JVP (either by physical examination or ultrasound) with prognosis in PH patients. One prior study found that elevated JVP on physical examination had a moderate sensitivity for the diagnosis of PH [9] but that JVP-exam underestimates invasively measured RAP. This has also been demonstrated for JVP-US in non-PH populations [5, 10], with underestimation of RAP by 0.5–5 cmH$_2$O. Interestingly, we found that JVP-US tended to be higher than JVP-exam.

Although the prospective design and the standardised protocols for measuring JVP-US and collecting clinical worsening events are strengths of our study, there are limitations that should be acknowledged. First, we did not have contemporaneous invasive measures of RAP, although this does not invalidate the importance of JVP-US in non-invasively predicting prognosis. Second, due the pragmatic nature of study, we included PH patients from all WSPH subgroups, although some outcomes (addition of PH medication, lung transplant) may not be relevant to those with non-group 1 PH (*e.g.* left-heart disease-PH). However, in a sensitivity analysis restricted to group 1 and 4 PH patients, JVP-US remained a significant independent predictor of TTCW. We chose to use the contemporary REVEAL 2.0 risk score since this is most widely used in practice; however, when using the original REVEAL score [11] for adjustment, which has been validated in non-WSPH group 1 PH [12], the results were unchanged (data not shown).

In conclusion, a simple, quick, and feasible ultrasound measure of JVP accurately predicted clinically relevant events in a broad group of PH patients independently of a robust predictor such as REVEAL risk score. If this is confirmed in other cohorts, JVP-US could be incorporated into outpatient PH practice.

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