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Original Article

Role of Internal Jugular Vein Ultrasound Measurements in the Assessment of Central Venous Pressure in Spontaneously Breathing Patients: A Systematic Review

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Background: Few studies have tested the role of the internal jugular vein (IJV) ultrasonographic (US) diameters in the assessment of central venous pressure (CVP) in spontaneously breathing patients. No review or meta-analysis is currently available on the role of IJV assessment in this setting. The aim of this systematic review is to check the reliability and accuracy of IJV US diameters in predicting CVP and to evaluate its correlation with CVP in spontaneously breathing patients.
Methods: This systematic review was based on the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. We included studies on the accuracy and reliability of the IJV ultrasound measures and studies exploring its correlation with CVP in adult spontaneously breathing patients. The studies' report quality was assessed by Standards for Reporting of Diagnostic Accuracy (STARD) and Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 scales.
Results: A total of five studies was eligible for final analysis. The studies on IJV ultrasound measures showed a good quality in reporting. The anterior-posterior diameter maximum of IJV (AP-IJV Dmax) showed the best correlation with the CVP with a good inter-rater reliability and validity in predicting CVP. All measures showed good inter-rater reliability and validity in predicting CVP, but only the AP-IJV Dmax showed good correlation with CVP.
Conclusions: The AP-IJV Dmax could be a potential surrogate of CVP because of its good reliability and validity in predicting CVP value and its fair-moderate correlation with CVP. Anyway, further research should confirm these conclusions.

Key words: *systematic review, internal jugular vein ultrasound, reliability, validity*

Introduction

The assessment of intravascular volume status (IVS) is one of the great challenges in the care of critically ill patients, particularly if presenting with shock. An accurate IVS evaluation is essential in this setting to properly manage fluid therapy and responsiveness to treatment. Vital signs, biochemical markers, invasive and non-invasive tests are all the available tools to monitor IVS, even though according to many experts dynamic measures better predict fluid responsiveness.[1-4] Although the central venous pressure (CVP) does not seem to predict the volume status,[4] many studies used it as a gold standard to

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manage fluid therapy. However, the changes of CVP values should not be used to test the fluid responsiveness.[4]

In the last years, the ultrasound has been suggested as a valid method to guide the diagnosis and therapy in shock patients.[3] Among the ultrasound measures used as IVS surrogates, the diameter of inferior vena cava has been proposed as a feasible measure of fluid responsiveness in critically ill patients.[2-6] The ultrasound assessment of IVC diameter and respiratory variations was included in the 2008 American College of Emergency Physicians (ACEP) Policy Statement on Emergency Ultrasound Guidelines as a tool for IVS and CVP evaluation. The value of this assessment is supported by the pathophysiological observation that total body fluid volume correlate with absolute IVC diameter, while the variations in intra-thoracic and intra-abdominal pressure during spontaneous breathing are able to induce IVC collapse and dilatation with inspiration and exhalation, respectively. The 2008 ACEP Policy Statement on Emergency Ultrasound Guidelines suggest measuring IVC inspiratory and expiratory diameter at 2 cm from its junction with the right atrium using a low-frequency probe (3.5–5 MHz) at the trans-abdominal subcostal view. The degree of inspiratory and expiratory diameters change is generally expressed as a percentage by the caval or IVC collapse index (CI) obtained by the IVC maximum diameter (IVC Dmax) minus the minimum (IVC Dmin) diameter of the IVC divided by the maximum diameter: IVC-CI = (IVC Dmax – IVC Dmin)/IVC Dmax. All these measures are obtained during one respiratory cycle (http://www.acep.org).

According to the ACEP Policy Statement on Emergency Ultrasound Guidelines, a "hypovolemic" patient presented a small IVC diameter and an IVC CI greater than 50%. In a recent review, Schmidt et al. suggested that a very small IVC diameter and a small and hyperkinetic left ventricle could be predictive of shock.[3]

Several studies have tested the relationship between the ultrasound measure of IVC diameters and the CVP,[7-11] but few reports are available in spontaneously breathing patients.[9,12,13] In particular, the IVC Dmax, IVC Dmin, the IVC distensibility, or caval index (IVC Dmax − IVC Dmin/IVC Dmax × 100, expressed as a percentage), IVC ratio (IVC maximum transversal/IVC maximum longitudinal) have been evaluated to estimate CVP mostly in spontaneously breathing critically ill patients bedside, during their admission to the emergency department or in patients undergoing right heart catheterization, but only few studies describe their scanning protocol and the inter-rater reliability.[9,12-17]

To our knowledge, few reports have been published on the role of internal jugular vein (IJV) ultrasonographic (US) measures as a tool to estimate the volume status and fluid responsiveness and to test their relation with the CVP.[9,11,18-20] The IJV ultrasound measures should be obtained according to the methods described by previous researchers[9,11,18] with the patient in the supine position and a high frequency (5–10 MHz, linear array) linear transducer lightly placed on the neck in a transverse plane over the IJV 2 cm above the clavicle. Using a B-mode cine loop is possible to obtain the anterior-posterior of IJV (AP-IJV) and the transverse diameter of IJV (T-IJV). The following ultrasound measures of IJV have been tested: AP-IJV Dmax; the IJV area (maximal area in transversal section); the IJV ratio: IJV maximum transversal/IJV maximum longitudinal.[9,10,18-20]

To summarize, very few reports have tested the effectiveness of IJV ultrasound measures among spontaneously breathing patients.

To our there are no reviews on the role of the IJV in the assessment of volume status. Moreover, the conclusions of the reports published on the reliability, validity, and correlation with the CVP of ultrasound measures of IVC and IJV are divergent. For these reasons, we decided to conduct this systematic review.

The primary aim of this review was to check the available studies exploring one of the following measures: (1) the reliability of IJV ultrasound measures; (2) the validity of IJV ultrasound measures in predicting CVP; (3) the IJV ultrasound measures correlation with the CVP in spontaneously breathing critically ill patients. Another purpose was to assess the quality of selected studies published on this topic.

Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement for reporting systematic reviews and meta-analyses.[21] The flow diagram in Fig. 1 schematically shows each step of the review process.

A broad search of the literature was initially performed by an expert in literature searching using

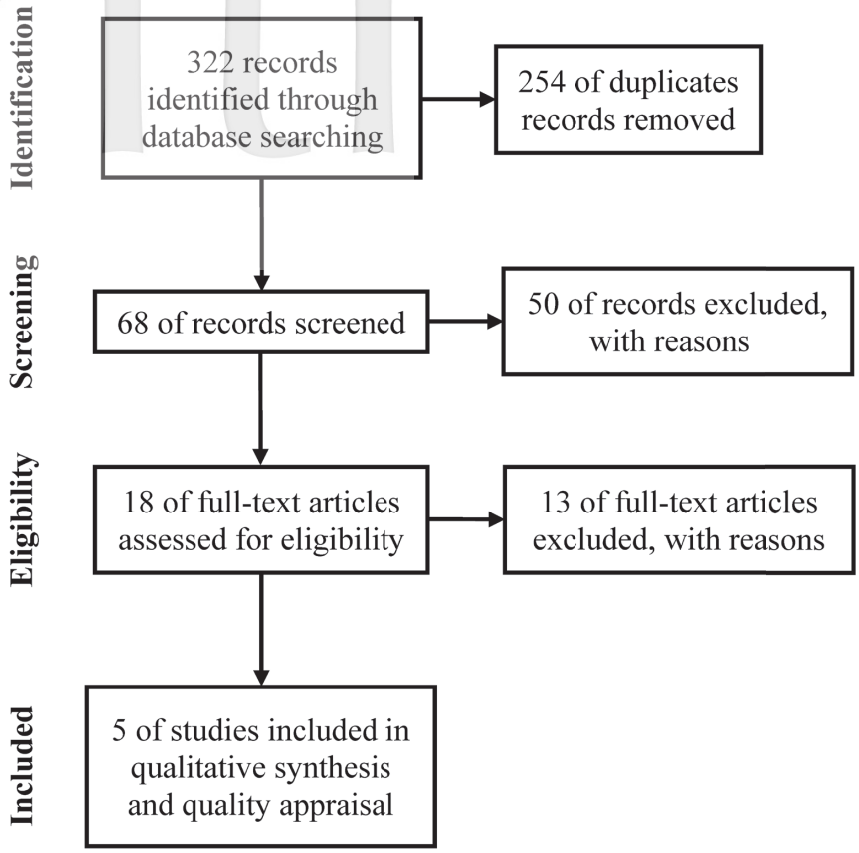

Fig. 1. Review selection process.

PubMed, Cochrane Library, Web of Science, and Scopus. All the articles available, starting from the year 1941 until the time of search (June 30, 2015), were considered.

An update of the literature search has been conducted from the June 1, 2016.

The literature search strategy and criteria are shown in Supplement 1.

A total of 322 records was retrieved (Fig. 1).

Three researchers independently and in a blinded manner reviewed the four lists from the literature database (PubMed, Cochrane Library, Web of Science, and Scopus), and by the records' title and abstract inspection, removed 254 duplicates and other 50 reports because they were not relevant to the aims of the review.

Eighteen full text articles were finally selected and independently reviewed by three researchers to identify those potentially relevant.

Only five studies met the inclusion criteria for the systematic review, exploring the correlation of IJV ultrasound measures with CVP and/or accuracy and/or reliability of US exams. The reasons for exclusion were justified in each phase of the selection.

An appraisal of the reporting quality of the five remaining studies selected for the analysis, was independently conducted by three authors using the Standards for Reporting of Diagnostic Accuracy (STARD)[22] and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2[23] guidelines.

A narrative summary was used to synthetize the data to provide a narrative description and ordering of the evidence, with commentary and interpretation.

The three reviewers' yes/no level of agreement for each study was entered into an Excel 2010 (Microsoft Corporation, Redmond, WA, USA) spreadsheet, and Fleiss' kappa for observed agreement was performed. We obtained a Fleiss' kappa score of $\kappa = 0.72$, equating to a high level of agreement between the raters.

Outcome measures were the following: (1) inter-rater and intra-rater reliability coefficients (tested using kappa coefficient, weighted and/or un-weighted, intraclass correlation coefficient, Pearson correlation coefficient, and Spearman's rank correlation coefficient);

(2) the validity of IJV ultrasound measures in predicting CVP (tested using the following accuracy indexes: accuracy, sensitivity, specificity measure; receiver operator characteristic (ROC) curves with areas under the ROC curves [AUCs]). The prediction, measured by AUC (ROC curve), is the ability of the test (IVC and IJV ultrasound) to correctly classify those with and without the CVP (i.e., CVP < 10 mmHg = 0; CVP > 10 mmHg = 1); (3) coefficient of determination of regression analysis (R^2); Pearson correlation coefficients (r) or Spearman rank correlation coefficients (rho). Correlation is a statistical technique that can show whether and how strongly pairs of continuous variables (i.e., IJV ultrasound diameters or CVP values) are related.

Inclusion criteria were studies which tested the following measures: (1) the reliability of IJV ultrasound measures; (2) the validity of IJV ultrasound measures in predicting CVP; (3) the IJV ultrasound measures' correlation with the CVP in spontaneously breathing critically ill patients.

We included studies conducted on all ages of adult patients (> 18 years) in all languages.

We excluded the duplicate studies.

Results

Out of a total pool of 322 collected records, five[9,11,18-20] studies were considered eligible for the analysis.

In this review, 233 patients have been enrolled, with an age mean range from 51 to 66 years; a percentage of male range from 45 to 63% (Table 1).

The study conducted by Prekker et al.[9] tested IVC and IJV ultrasound measures.

Many studies on IJV ultrasound measures showed good quality in reporting according to STARD guidelines (Fig. 2) and all records had similar quality according to QUADAS-2 tool (Table 2).

Among the reports included: four tested the correlation with CVP of IJV ultrasound diameters; five tested IJV validity in predicting CVP; three the reliability of IJV. All the studies on IJV enrolled spontaneously breathing patients.

The following ultrasound measures of IJV have been tested in the included studies: AP-IJV diameter (two studies); IJV area (two studies); IJV ratio (two studies).

The comparison of effectiveness of IJV ultrasound measures is shown in Table 3.

There are no reports on the reliability of IJV ratio (Table 3).

The AP-IJV Dmax showed the best correlation with the CVP: r = 0.82 (Table 3).

All ultrasound measures of IJV showed good validity in predicting CVP; the AP-IJV Dmax and IJV area showed good inter-rater reliability.

Discussion

Few studies have been published on the relationship between the ultrasound measures of IJV diameters and the CVP as well as their reliability.

In this systematic review, the AP-IJV Dmax and IJV area showed the best correlation with the CVP, the best validity in predicting its values and a very good inter-rater reliability.

However, we should be prudent when we use the CVP and the IJV ultrasound measures to manage fluid resuscitation because a recent meta-analysis[4] showed that the CVP does not seem to predict the volume status.

Furthermore, we should be cautious in interpreting the IJV ultrasound measures in some clinical contexts.

For example in patients with cor pulmonale, a high IJV diameter and a reduced caval index does not exclude fluid responsiveness.

In this clinical context, even CVP has the same problems of IJV, of being unreliable in predicting fluid responsiveness. For this reason, the specificity of IJV would have been lower if considering prediction of fluid responsiveness compared to CVP.

Our findings suggest that the AP-IJV Dmax and its area could be two new indexes useful in the management of fluid in resuscitation. In fact, both show good reliability and validity in predicting CVP values. Few recommend that further research should confirm these conclusions because existing research on these ultrasound measures is insufficient.

In particular further studies are needed assessing IJV in predicting fluid responsiveness.

To our knowledge, there are not reviews on the role of IJV ultrasound measures in the assessment of volume status and fluid responsiveness in critically ill patients.

However, it is difficult to compare the results of studies collected on this topic because of their different designs and statistical methodologies used to test the outcomes.

In our opinion, because the authors of studies included have chosen different thresholds to test the

Table 1. Characteristics of studies on internal jugular vein[a]

Author	Study design	Target population	US measures	Outcome	Results	Conclusion
Prekker et al., 2013[9] USA	Cross-sectional	44 adult spontaneously breathing patients	IJV ratio[b]	ROC curves Linear regression analysis	R^2 = 0.21 for IJV ratio[b] Accuracy of IJV in predicting CVP < 10 mmHg: AUC = 0.76 (95% CI = 0.65–0.89)	Poorly correlation Moderate validity
Keller et al., 2009[11] USA	Prospective observational	44 adult spontaneously breathing patients	IJV ratio[b]	Intra and inter observer agreement (Bland-Altman plots) ROC curves	Accuracy of IJV in predicting CVP < 8 mmHg: AUC = 0.84 (95% CI = 0.72–0.96)	Inter and intra-rater reliability moderate IJV ratio[b] accurately estimates CVP = 8 mmHg
Donahue et al., 2009[18] USA	Prospective observational	34 adult spontaneously breathing patients	AP-IJV IJV area[c]	Inter-rater reliability Correlation between CVP and ultrasound IJV measures (in several decubitus and respiratory cycle)	Correlation of CVP and IJV supine position and at the end of Expiration and IJV area[c]: r = 0.82 and 0.69 IJV interclass correlation coefficient between the 2 observers = 0.92	Reliability excellent If AP-IJV diameter < 7 mm then CVP < 10 cmH_2O
Siva et al., 2012[19] Australia		44 adult spontaneously breathing patients	AP-IJV	ROC curves Pearson correlation	Significant correlation of anterior-posterior RIJV with CVP Accuracy of RIJV in predicting CVP, for overvolumed AUC = 0.73 (95% CI = 0.59–0.86), for undervolumed AUC = 0.83 (95% CI = 0.70–0.96)	Significant correlation and validity
Simon et al., 2010[20] USA		67 adult spontaneously breathing patients	IJV area[c]	ROC curves Reliability (inter-intra rater) Pearson correlation	Accuracy of RIJV area (with Valsalva) in predicting high RAP (> 12 mmHg): AUC = 0.86 (95% CI = 0.75–0.97) No significant correlation between resting RAP and RIJV CSA (r = 0.14) RIJV area: ICC intra = 0.88; ICC inter = 0.93	Intra- and inter-rater reliability very good

AP-IJV: anterior-posterior of internal jugular vein; AUC: areas under the receiver operator characteristic curves; CI: confidence interval; CSA: cross-sectional area; CVP: central venous pressure; ICC: intraclass correlation coefficient; IJV: internal jugular vein; RAP: right atrial pressure; RIJV: right internal jugular vein; ROC: receiver operator characteristic; US: ultrasonographic.
[a]Test characteristic: sensitivity, specificity, positive and negative predictive values.
[b]The IJV ratio: IJV maximum transversal/IJV maximum longitudinal.
[c]The IJV area: maximal area in transversal section.

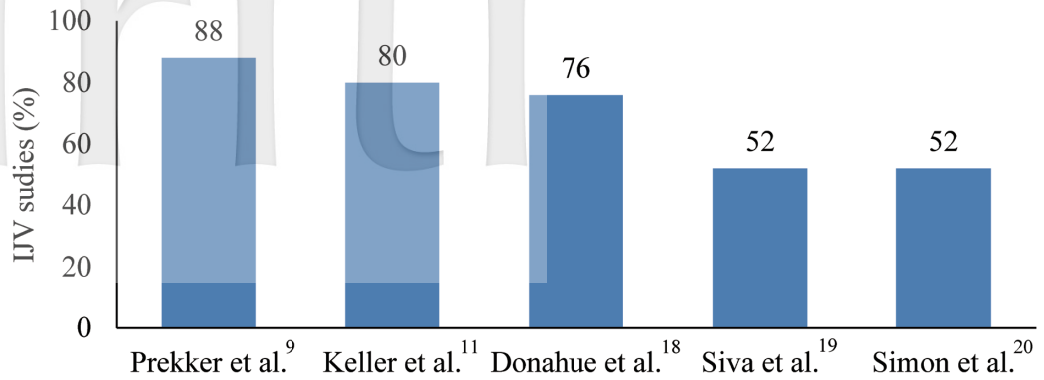

Fig. 2. Comparison of quality of reporting among studies on internal jugular vein (IJV) (Standards for Reporting of Diagnostic Accuracy [STARD] results). The vertical axis shows the percentage of items from STARD score met by each study according to the judgement of three researchers who checked each report using the STARD tool.

Table 2. Quality Assessment of Diagnostic Accuracy Studies-2 results

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Prekker et al., 2013[9]	HR	LR	HR	LR	LR	LR	LR
Keller et al., 2009[11]	LR	LR	HR	LR	LR	LR	LR
Donahue et al., 2009[18]	LR	UR	HR	LR	LR	LR	LR
Siva et al., 2012[19]	UR	UR	LR	LR	LR	LR	LR
Simon et al., 2010[20]	LR	LR	HR	LR	LR	HR	HR

HR: high risk; LR: low risk; UR: unknown risk.

Table 3. Comparison of internal jugular vein ultrasound measures effectiveness[a]

	AP-IJV	IJV ratio[b]	IJV area[c]
Reliability			
Inter-rater	[18]ICC = 0.92		[18,20]ICC = 0.92–0.93
Reliability			
Intra-rater			[20]ICC = 0.88
Correlation with CVP	[18]r = 0.82	[9]R^2 = 0.21	[18]r = 0.69
Validity in predicting CVP or overvolume or undervolume[d]	[19]AUC = 0.73 (95% CI = 0.59–0.86) [19]AUC = 0.83 (95% CI = 0.70–0.96)	[9]AUC = 0.76 (95% CI = 0.65–0.89) [11]AUC = 0.84 (95% CI = 0.72–0.96)	[20]AUC = 0.86 (95% CI = 0.75–0.97)

AP-IJV: anterior-posterior of internal jugular vein; AUC: areas under the receiver operator characteristic curves; CI: confidence interval; CVP: central venous pressure; ICC: intraclass correlation coefficient; IJV: internal jugular vein.

[a]The numbers near each value are the studies' reference number which report the variables shown in the table.

[b]The IJV ratio: IJV maximum transversal/IJV maximum longitudinal.

[c]The IJV area: maximal area in transversal section.

[d]The authors tested the IJV's validity in predicting CVP using several cut-off: CVP < or > 10 mmHg; CVP < or > 12 mmHg; < or > 8 mmHg. In particular the AP-IJV has been tested for undervolume (AUC = 0.83) and overvolume (AUC = 0.73);[19] the IJV ratio has been tested for CVP < 10 mmHg (AUC = 0.76) and CVP < 8 mmHg (AUC = 0.84);[9,11] the IJV area for CVP >12 mmHg (AUC = 0.86).[20]

accuracy of IJV in predicting the CVP (Table 1), it is not possible to combine their results using a forest plot method.

Even though the studies included in the systematic review showed a moderate-good quality in reporting, especially according to QUADAS-2 guidelines.

Several limitations should be noted in the results of this review.

Firstly, a very small number of patients was enrolled in all the studies collected and secondly there was significant heterogeneity among patient populations, inclusion and exclusion criteria, design, and statistical methodology employed in each study: this could be a very important limitation in terms of reaching conclusions from this review.

Moreover, only few studies supported the findings and conclusions on the AP-IJV and IJV area.

Finally, because there are very few data on the reliability of the IJV ultrasound measurements and there could be a great operator-dependent variability, we should be very cautious before using these US indexes in clinical practice.

On the other hand, this systematic review is original because for the first time, data on the role of IJV in fluid management in critically ill patients has been collected. Moreover, to our knowledge, this is the first systematic review on the reliability of ultrasound measures of IJV. Finally, there are no existing reviews or meta-analyses on the comparison of performance of these ultrasound measures.

Although recent literature[4,24,25] suggests that CVP measurements do not accurately predict volume responsiveness, many International Society of Emergency and Critical Care suggest to use the CVP to manage the patients in shock[26,27] and the CVP remains the most frequently used variable to guide fluid resuscitation in critically ill patients.[28]

Moreover, many studies used CVP as gold standard to compare other indices to predict volume responsiveness.

Finally, according to De Backer and Vincent's opinion, the CVP values provide important information about the cardiocirculatory status of the patient and should not be abandoned.[29]

For these reasons, we think that our findings on the effectiveness of IJV as a surrogate of CVP could impact the actual clinical practice; as they support the role of ultrasound to guide clinical management of patient in shock[3] and support further research on new ultrasound measures as AP-IJV which could be a useful, fast, and safe tool to provide rapid fluid resuscitation early in the course of shock. The IJV ultrasound examination could be used in several settings by the emergency department physician, specifically when the IVC ultrasound method is not feasible because of poor acoustic windows (obesity, abdominal air interposition, surgical wounds).

Moreover, both IJV and IVC ultrasound measures are a very convenient method not requiring extensive training or expensive equipment.

However, the volaemic status is probably better assessed by an integrated sonographic approach with IVC and IJV, cardiac and pulmonary ultrasound.

In conclusion, the findings of this systematic review seem to suggest that the AP-IJV Dmax could be a good surrogate of CVP because of its good validity in predicting CVP but its correlation with CVP value among the studies collected is fair-moderate. Further studies should test its reliability.

Finally, the AP-IJV Dmax and its area could be a promising alternative to be confirmed by future research on their effectiveness.

Conflicts of Interest Statement

The authors declare that they have not had conflicts of interest within the 36 months of submission.

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Supplement 1. Literature search: strategy and criteria

The following key words and strategy were used for the literature search.

(1) One search was performed using PubMed

Search field title: ((jugular veins[mesh] OR "internal jugular vein") AND ultrasonography) AND (blood volume[mesh] OR "blood volume" OR "volume status" OR "volemic status" OR central venous pressure[Mesh] OR "central venous pressure"): 87 records.

(2) One search was performed using Web of Science

Search field title: Internal jugular vein AND (blood volume OR volume status OR volemic status OR central venous pressure): 117 records.

(3) One search using Scopus

Search field title: ((TITLE-ABS-KEY(internal jugular vein AND ultrasonography) AND TITLE-ABS-KEY(blood VOLUME))) OR ((TITLE-ABS-KEY(internal jugular vein AND ultrasonography) AND TITLE-ABS-KEY(central venous pressure))) OR ((TITLE-ABS-KEY(internal jugular vein AND ultrasonography) AND TITLE-ABS-KEY(volemic status))) OR ((TITLE-ABS-KEY(internal jugular vein AND ultrasonography) AND TITLE-ABS-KEY(VOLUME status))): 116 records.

(4) One search using Cochrane Library

Search field title: internal jugular vein ultrasound: 2 records.

A total of 322 records were selected at the end of this research.