Point-of-care multi-organ ultrasonography for the evaluation of undifferentiated hypotension in the Emergency Department

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ABSTRACT

Purpose: We analyzed the efficacy of a point-of-care ultrasonography protocol, based on a focused multi-organ examination, for the diagnostic process of symptomatic, non-traumatic hypotensive patients in emergency.

Methods: We prospectively enrolled 108 adult patients complaining of non-traumatic symptomatic hypotension of uncertain etiology. Patients received immediate point-of-care ultrasonography to determine cardiac function and right/left ventricle diameter rate, inferior vena cava diameter and collapsibility, pulmonary congestion, consolidations and sliding, abdominal free fluid and aortic aneurysm, leg veins thrombosis. The organ oriented diagnoses were combined to formulate an ultrasonography hypothesis of the cause of hemodynamic instability. Ultrasonography diagnosis was then compared with a final clinical diagnosis obtained by agreement of three independent expert physicians, who performed a retrospective hospital chart review of each case.

Results: Considering the whole population, concordance between the point-of-care ultrasonography diagnosis and the final clinical diagnosis was interpreted as *good*, with Cohen's k = 0.710 (95% CI, 0.614-0.806), $p < 0.0001$ and raw agreement (Ra) = 0.768. By eliminating the 13 cases where the final clinical diagnosis was not agreed (indefinite), the concordance raised to *almost perfect*, with k = 0.971 (95% CI, 0.932-1.000), $p < 0.0001$ and Ra = 0.978.

Conclusions: Emergency diagnostic judgments guided by point-of-care multi-organ ultrasonography in patients presenting with undifferentiated hypotension, significantly agreed with a final clinical diagnosis obtained by retrospective chart review. The integration of an ultrasonography multi-organ protocol in the diagnostic process of undifferentiated hypotension has a great potential in guiding the first-line therapeutic approach.

Trial registry: ClinicalTrials.gov; No.: NCT01572571; URL: www.clinicaltrials.gov

KEY WORDS: hypotension; shock; ultrasonography; diagnosis.

INTRODUCTION

A differential diagnosis is a systematic procedure that allows physicians to identify a condition where multiple alternatives are possible. In case of medical emergencies, there may not be enough time to perform detailed diagnostic procedures, in which case the main purpose of a differential diagnosis is to eliminate from the probabilities any imminently life-threatening condition. Point-of-care ultrasonography in the hands of the clinician is a safe, rapid, non-invasive diagnostic technique, suitable for use at the bedside, that can help physicians to answer time-dependent focused clinical puzzles and accelerate greatly the differential diagnostic procedure [1]. The potential of point-of-care ultrasonography in emergency is rapidly growing and is having continuous innovation in recent years. Examples of these innovations are implementation of a focused cardiac and lung ultrasonography evaluation in the procedures for the early diagnosis in the extreme emergencies [2]. Particularly, lung sonography represents a novelty in the hemodynamic evaluation and monitoring of the critically ill [3, 4].

Undifferentiated hypotension is a common condition in the Emergency Department (ED), recognized as a strong predictor of in-hospital mortality [5, 6]. A safe and early goal-directed supportive treatment of hypotensive patients depends on identification of possible etiologies and a prompt exclusion of the most severe and rapidly fatal conditions. Point-of-care ultrasonography plays an important role in the diagnostic procedure of undifferentiated hypotension in the emergency setting. Some protocols consisting in a goal-directed ultrasonography evaluation that integrate cardiac, abdominal and venous examination, have been already proposed and validated [7-9]. Some review articles already introduced the adjunct of a lung evaluation in the multi organ ultrasonography diagnostic procedure of undifferentiated hypotension and shock, but have not been validated by prospective studies on patients [10-14].

The purpose of the present study is to validate a rapid focused ultrasonography protocol that incorporates a bedside stepped examination of heart, inferior vena cava, lung, abdomen and leg veins as part of a point-of-care examination, for the early approach to non-traumatic undifferentiated hypotension in emergency. Hypothesis of the study is that early diagnostic predictions guided by ultrasonography, would significantly agree with retrospective diagnoses performed by chart review of three independent expert clinicians. A secondary objective is to evaluate the number of cases where lung examination, incorporated in a multi-organ ultrasonography protocol, is decisive to obtain a definite diagnosis.

METHODS

Enrollment

We prospectively enrolled 114 patients from May 2011 to December 2012 in the Emergency Department (ED) of San Luigi Gonzaga University Hospital in Torino, Italy, an urban 400-bed teaching hospital. The ED serves the population of the west part of the town with >48000 visits per year. Criteria for enrollment included the following: 1) age >18 yrs and <95 yrs; 2) systolic blood pressure stably <100 mmHg at presentation, confirmed after at least 3 measurements during the first evaluation; 3) presence of at least one of the following signs or symptoms of hypo-perfusion: unresponsiveness, altered mental status (including unexplained severe anxiety), syncope, respiratory distress, profound asthenia with fatigue and malaise, severe chest or abdominal pain. Patients were excluded from the study in case of: 1) usual "low blood pressure" state reported by the patient or recorded in the history; 2) resuscitation maneuvers, with or without the use of defibrillation or ALS medications, before enrollment and invasive ventilation; 3) severe abdominal or thoracic trauma in the 24 hrs before enrollment; 4) ST elevation myocardial infarction at electrocardiogram or clear clinical signs of probable non-ST elevation myocardial infarction; 5) a clear cause of shock diagnosed before the ultrasonography evaluation, mandating prompt life-saving treatment, like external bleeding, active gastrointestinal bleeding, drugs overdose; 6) onset of signs and symptoms of shock during the hospital stay or in the ED after the initial evaluation. Criteria for inclusion and exclusion were blindly evaluated by at least two independent physicians at presentation, the attending physician and the ultrasonography operator, and only in case of a perfect concordance we proceeded with enrollment. Initial arterial blood pressure was measured in the ED triage area or, upon arrival, in the shock room of the high acuity section of the ED, and then monitored by automated oscillometric devices Solar 8000M (GE Healthcare, Milwaukee, WI, USA). The study protocol was reviewed and approved by the local Institutional Review Board (n. 182/2012) and the study registered at ClinicalTrials.gov (NCT01572571), and have therefore been performed in accordance with the ethical standards. A delayed written informed consent for the use of personal data was signed at a time when the patients were deemed competent. Next of kin participated to the informed consent procedure when needed.

All patients immediately received standard diagnostic emergent interventions including physical examination, intravenous access for whole blood assays, arterial gas analysis, electrocardiography, continuous cardiac monitoring, supplemental oxygen, supine chest radiography.

Ultrasonography technique

A point-of-care ultrasonography examination is routinely performed in all the unstable patients in our ED. For the purpose of the present study, an independent physician, unaware of all the other diagnostic tests and aware of visible physical signs and symptoms, performed the ultrasonography evaluation immediately upon arrival. The operator recorded the presence or absence of ultrasonography findings using an explicit list (Table1). Then, based on a combination of ultrasonography signs, the operator chose the diagnosis of the probable condition causing hypotension from a list of 9 possible ultrasonography patterns (Table2). All goal-directed ultrasonography studies were performed in two-dimensional gray scale with the patient in a supine to 30° upright position, using a Esaote MyLab 40 ultrasound system (Esaote Italia, Milan, Italy). The operator was a board-certified emergency physician with specific competence in emergency ultrasonography, performing about 400 emergency studies per year from no less than 5 years.

The standardized multi-organ ultrasonography protocol consisted of the study of the heart, inferior vena cava, lung, leg veins and abdomen, by using the views listed below.

Cardiac views: a cardiac phased array 2-4 MHz probe was used for the study of the heart through the subcostal, parasternal long axis and the apical four-chamber views. The subcostal four-chamber view was examined for fluid collection within the pericardial sac, right atrium/ventricle (RV) diastolic collapse, left ventricle (LV) impaired function by visual estimation of gross wall contraction and wall thickening, or LV hyperkinesia with impaired filling, RV dilation (RV/LV end diastolic diameter > 0.7) and visual estimation of impaired function [15-17]. At least one of other two cardiac views were used in case of doubtful diagnosis, difficult visualization and for confirmation of RV dilation. The parasternal long axis was examined for pericardial effusion, visual estimation of qualitative LV function, signs of RV dilation (RV/LV end diastolic diameter > 0.7) [17]. The apical four-chamber view was examined for pericardial effusion, qualitative LV function and signs of RV dilation (RV/LV end diastolic diameter > 0.9) [18-20].

Lung views: the same probe used for cardiac study or, alternatively, a curvilinear 2-5 MHz probe was used for intercostal lung views (oblique scans). Fundamental ultrasonography signs were considered multiple B-lines, subpleural consolidations, air bronchograms and lung sliding. The standardized eight anterior-lateral areas examination was used [21]. Absence of multiple B-lines with regular sliding is the “A pattern”, which is a sign of normally aerated or hyper inflated lungs and rules out pulmonary edema and pneumothorax. Multiple B-lines on at least two scans per side represent the “B pattern”, a sign of diffuse interstitial syndrome. This condition indicates cardiogenic pulmonary congestion, or, alternatively, lesional edema in ARDS, pulmonary fibrosis, interstitial pneumonia [22]. Detection of multiple B-lines limited to less than two scans per side or limited to one side is the “A/B pattern”, a sign of focal interstitial syndrome. This condition indicates a focal interstitial involvement around isolated pulmonary consolidations, like pneumonia, infarction, contusion [3]. Pulmonary consolidations with air bronchogram indicate consolidative processes of the lung, very often due to pneumonia [23, 24]. The examination was extended also to the dorsal areas to visualize possible posterior consolidations. Respiratory lung sliding was also checked, and its absence with absence of B-lines, lung pulsation and images of consolidation, was considered sign of tension pneumothorax [25]. For brevity, in the text and tables this set of signs is indicated “no sliding”. Diagnostic criteria corresponded to the recommendations of the recent consensus conference on lung ultrasound [21].

Inferior vena cava views: the subcostal view was used for long axis visualization of the proximal inferior vena cava (IVC) to measure maximum diameter, estimate percent of respiratory collapsibility (caval index), visualization of intra-luminal thrombosis. The same probe used for cardiac views or, alternatively, a curvilinear 2-5 MHz probe was used. All measurements were made no less than 2 cm caudal from the junction of the right atrium [26]. The pattern considered significant for central venous pressure (CVP) >10 mm Hg coincided with diameter >2 cm and absent or reduced (<40%) collapsibility, while low CVP (<5 mm Hg) was diagnosed with diameter <2 cm and total or enhanced collapsibility (>50%) [27, 28]. All the intermediate conditions were considered not diagnostic. A third condition interpreted as sign of acute overload was visualization of spontaneous echo contrast (sludge) or solid echogenic thrombi [29].

Abdominal views: free fluids were estimated by curvilinear 2-5 MHz probe, as detection of anechoic free spaces in the traditional peritoneal pouch [30]. The anterior-posterior diameter of the abdominal aorta was measured in the short axis view and a measure >30 mm was considered sign of dilation [31].

Leg veins views: the common femoral and popliteal leg veins were examined for collapsibility in short axis using a linear 7-12 MHz probe. Absence of collapsibility was considered diagnostic for intra-luminal thrombosis [32]. In case of negative examination but strong suspicion for thrombosis, the bilateral venous waveform was analyzed by color-doppler to check for asymmetry indicating proximal obstruction [29].

Each ultrasonography examination was performed by following a systematic and standardized sequence: heart, inferior vena cava, lungs, abdomen, legs veins. If the cause of hypotension was obvious at any point of the ultrasonography evaluation, the examination was concluded. The physician having in charge the patients' care was always aware of the ultrasound findings obtained during our first line examination, and used the information for the immediate diagnostic and treatment decision making.

Retrospective clinical evaluation

The aim of retrospective clinical evaluation was to establish a final clinical diagnosis using a predefined, structured method of chart review. Three expert board-certified clinicians (FM, emergency physician, PR, cardiologist and CL, radiologist) examined all relevant clinical documentation of cases, including laboratory data, imaging procedures, consultative calls, post-mortem evaluation, and other data recorded during the hospital stay. The auditors were blinded to the results of the initial ultrasonography evaluation, and their chart review consisted of three separate steps. Initially, inclusion criteria of each single case were re-discussed. Cases where criteria of enrollment were not considered fully respected, where excluded from a further clinical evaluation. Then, each auditor independently formulated a personal clinical diagnosis of the initial cause of undifferentiated hypotension, by choosing from a list of 8 possible diagnoses. These clinical diagnoses correspond to the ultrasonography categories listed in table 2, with the exception of the *distributive/hypovolemic*. They represent widely accepted definitions for the diagnosis of non-traumatic hypotensive state, as published in specialty textbooks [33, 34]. Cases where the clinical documentation was considered not complete or insufficient, were concluded as *indefinite*. Finally, the committee of auditors, in plenary meeting, discussed the cases where the three independent personal diagnoses were not concordant. When the plenary discussion did not create full consensus, contradictory was concluded by majority. Cases without agreement of at least two of the three auditors, were concluded as *indefinite*.

Statistical evaluation

Continuous data are presented as mean ± SD. The ultrasonography diagnoses were compared with the respective final clinical diagnoses by employing the Cohen *k* inter-rater coefficient of agreement [35]. Values assumed by the coefficient in the different types of analyses performed are reported with the 95% confidence intervals, the p-value for the significance and the corresponding raw-agreement index. We followed the 6 categories of interpretation of the *k* coefficient values [36]. For statistical hypothesis tests, $p < 0.05$ was considered significant. The sample size was estimated to detect an accuracy of our protocol >90%, requiring an enrollment of approximately 40 patients. However, the sample necessary for using the kappa method is at least 90 cases. Anticipating an approximately 10% rate of exclusion, we planned a sample size of >100 patients.

RESULTS

Of the 114 patients enrolled, six were excluded: one patient had a significant difference in the measured arterial pressure between the two arms, documentation of other two patients was considered not complete by the review board and for the remaining three patients, history records revealed they were chronically hypotensive. Thus, the study sample size was 108 patients, 66 men, 42 women, with an average age of 71.5 ± 13.5 yrs, and a systolic blood pressure at presentation 84 ± 11.0 mmHg. Seven patients died during hospital stay, and 3 of them were autopsied. The average time needed for a complete ultrasonography evaluation was 4.9 ± 1.3 min. The final charted hospital diagnoses of the 108 cases are reported in Table 3. The final clinical diagnoses based on chart assessment by the three auditors and the ultrasonography diagnoses obtained in the 108 patients, are shown in Table 4. In the period of the study there were no cases of tension pneumothorax.

Eighteen out of 67 patients with *hypovolemic* or *distributive* ultrasonography diagnoses did not show signs of hyperkinetic left ventricle, but showed the A pattern at lung ultrasonography. One out of the 15 cases with *cardiogenic* diagnosis at ultrasonography did not show hypokinetic left ventricle, but showed pulmonary B pattern. Three out of 8 patients with an ultrasonography diagnosis of pulmonary embolism did not show signs of inferior vena cava congestion, but showed pulmonary A pattern. Lung ultrasonography was also decisive to finalize the diagnosis of a *mixed* pattern in 3 out of 8 cases. Overall, incorporation of a lung examination in our multi-organ ultrasonography protocol was decisive for a definite diagnosis in 24 cases (22%).

Lung ultrasonography detected signs of pulmonary consolidation in 30 patients, in 18 cases showing also air bronchogram. Of these, 25 had a definite diagnosis of *distributive* hypotension and 3 *mixed*, with *distributive* as one of the two components.

We performed three analyses: analysis 1 consisted of comparing the ultrasonography diagnoses with the final clinical diagnoses for all the 108 cases. The ultrasonography *hypovolemic/distributive* pattern was considered concordant to the final clinical diagnosis when this latter was *hypovolemic*, *distributive* or *mixed distributive/hypovolemic*. Analysis 2 was similar to the first, but in case of a *mixed* clinical diagnosis with a combination of two categories, the ultrasonography diagnosis was considered concordant when it was the same of at least one of the two. For analysis 3 we used the same criteria of the second, but excluded the cases with *indefinite* final clinical diagnosis (n = 13) and *indefinite* ultrasonography pattern (n = 7). They were 16 cases overall, because 4 cases were *indefinite* for both the ultrasonography operator and the committee of auditors. Thus, analysis 3 was possible on 92 patients. Data from analysis 1, 2 and 3 are shown in Table 5.

DISCUSSION

Goal-directed ultrasonography is an excellent diagnostic methodology to evaluate the etiology of undifferentiated hypotension at bedside. Basic focused ultrasonography study of single organs can provide important information on functional changes. Combining single ultrasonography analyses in a rapid multi-organ protocol improves accuracy of the diagnostic process in case of challenging clinical situations, like undifferentiated hypotension, sepsis and cardiac arrest. This potential was already introduced in some review articles and case series [2, 8, 9, 12, 14, 37], but efficacy was also demonstrated by prospective studies [7, 38]. On the basis of the recommendations of the main experts on point-of-care lung ultrasound [21], we added a pulmonary evaluation to a multi-organ ultrasonography protocol based on cardiac, veins and abdominal rapid examination of undifferentiated hypotension in emergency [7].

Our protocol was effective in guiding a safe first approach to undifferentiated hypotension in emergency, at least in good agreement with a detailed diagnostic evaluation performed by a retrospective chart review. Ultrasonography examination of the lung may add some crucial information in a multi-organ protocol in hypotensive states. In our study, lung examination was decisive to conclude a definite diagnosis in 24 patients. Lung ultrasonography may indicate both the hemodynamic effects of the condition on the pulmonary circulation, like pulmonary edema from *cardiogenic* shock, but also the presence of primitive pulmonary diseases causing hemodynamic instability, like pneumonia in sepsis.

The main goal of an early diagnostic ultrasonography study of undifferentiated hypotension cannot be the final diagnosis. Rather, point-of-care ultrasonography should be targeted at ruling-out any immediate life-threatening condition and identify the most likely cause of hemodynamic instability at that precise moment. For this reason, the committee of clinical auditors had to formulate the hypothesis on the main cause of the condition at presentation, which was not necessarily coinciding with the final charted hospital diagnosis. The need to separate the initial condition from the evolution of the disease was made sometimes complicated by the acquisition of the many data of the whole clinical documentation. These difficulties may explain some of the few discrepancies found between the initial ultrasonography hypothesis and the final clinical diagnoses.

The therapeutic interventions of undifferentiated hypotension at presentation can vary largely from the massive administration of fluids with amine support in case of hypovolemic and *distributive* causes, to the fibrinolysis or the invasive procedures in case of the *obstructive* causes, to the pharmacological and procedural treatment of the *cardiogenic* cause. Not only a missing diagnosis can be highly dangerous at an early phase, as when cardiac tamponade or pneumothorax are misdiagnosed. But also an erroneous therapeutic approach can be deleterious. For instance, massive fluid administration in case of *cardiogenic* hypotension with impaired global function of the left ventricle may rapidly precipitate the clinical condition. The use of point-of-care ultrasonography may allow immediate classification of the clinical condition into one of the pathophysiological categories or, at least, a prompt exclusion of an immediate life threatening condition. Further studies are needed to verify if a multi-organ point-of-care ultrasonography approach has a significant impact in the life expectancy of patients presenting with undifferentiated hypotension.

A limitation of our study is that we simplified our statistical analysis by arbitrarily corresponding the mixed *hypotensive/distributive* ultrasonography pattern to either the *hypovolemic* or *distributive* final clinical diagnoses. We based our ultrasonography differentiation between *hypovolemic* and *distributive* on the presence of a pulmonary consolidation with air bronchograms that may represent a site of infection. While ultrasonography signs of lung consolidation allowed a correct *distributive* diagnosis in most cases, this criterion has many limitations mainly because we may have a distributive condition without a pulmonary infection. However, this differentiation is theoretical since *hypovolemic* and *distributive* causes of undifferentiated hypotension need the same first-line therapeutic interventions to sustain hemodynamic. On the clinical grounds, a correct differentiation about these two categories not always is possible. The progressive aging of the general population leads to en ever-increasing access of elderly patients to our EDs. These patients represent a diagnostic challenge because very often they are multi pathological. Simplification of the diagnostic methodology is mandatory to match the complexity and variability of the daily practice in a crowded ED.

Another limitation is that our protocol does not incorporate pleural effusion, although lung ultrasonography has a great potential in the diagnosis of this condition. However, anechoic pleural fluid can never be assigned with certainty to a *cardiogenic* pattern because transudate cannot be differentiated by exudate using lung ultrasonography [21].

This study does not take into consideration training aspects for critical care ultrasonography. The expertise and skill of the ultrasonography operator is crucial for the maintenance of sufficient levels of diagnostic accuracy in critical care and should always be considered in the analysis of our data [39].

CONCLUSION

This study demonstrates that point-of-care ultrasonography diagnoses obtained in emergency agree with a post-hoc clinical analysis of the etiology of symptomatic undifferentiated hypotension. An ultrasonography protocol that includes lung examination may simplify the diagnostic process by reducing the viable diagnoses of hypotensive states, and may allow immediate diagnosis of life threatening conditions that can be reversed by prompt therapeutic interventions. Our data encourage the incorporation of ultrasonography into the routine emergency evaluation of undifferentiated hypotension to guide early interventions. Whether or not this approach influences the outcome of hypotensive patients and associated management costs and how to incorporate point-of-care ultrasonography in the diagnostic work-up, remain to be elucidated by further research.

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Table 1: Ultrasound sign evaluated in patients with undifferentiated hypotension.

	Y	N	I	NE
HEART				
Pericardial effusion with tamponade				
Hyperkinetic left ventricle				
Hypokinetic left ventricle (moderate or severe)				
Dilated and/or hypokinetic right ventricle				
INFERIOR VENA CAVA				
Max diameter <2 cm and respiratory collapse >40-50%				
Sludge or max diameter >2 cm and respiratory collapse <50%				
LUNGS				
A pattern (absence of multiple B lines)				
B pattern (multiple B lines diffuse and bilateral)				
B pattern with lung consolidation				
A/B pattern (focal B lines)				
Lung consolidation with air bronchogram				
No sliding, no pulse, no B-lines, no consolidation				
ABDOMEN				
Peritoneal free fluid				
Aortic aneurysm				
PERIPHERAL VEINS				
Deep vein thrombosis (no collapsibility femoral or popliteal)				

Y=Yes; N=No; I=Indefinite; NE=Not Evaluated.

Table 2: The list of 9 possible ultrasound patterns diagnosed in patients admitted for undifferentiated hypotension, and corresponding combination of findings detected at multi-organ point-of-care ultrasonography evaluation.

Ultrasound Pattern	***Organ evaluation***	***Corresponding signs***
Hypovolemic	Heart	*Hyperkinetic LV
	Inferior Vena Cava	*Diam. <2cm + Resp. collapse >50%
	Lungs	*A pattern
	Abdomen	*Free fluids/Aortic aneurysm
Distributive	Heart	Hyperkinetic LV
	Inferior Vena Cava	Diam. <2cm + Resp. collapse >50%
	Lungs	**B pattern with consolidation or consolidation with air bronchograms
Hypovolemic/Distributive	Heart	*Hyperkinetic LV
	Inferior Vena Cava	*Diam. <2 cm + Resp. collapse >50%
	Lungs	*A/B pattern
	Abdomen	*Free fluids
Obstructive Cardiac Tamponade	Heart	Pericard. effusion with tamponade
Obstructive Pulmonary Embolism	Heart	*Dilated/Hypokinetic RV
	Inferior Vena Cava	*Sludge or no respiratory collapse and max diam. >2 cm
	Lungs	*A pattern
	Peripheral Veins	*Deep vein thrombosis
Obstructive Tension Pneumothorax	Heart	Dilated/Hypokinetic RV
	Inferior Vena Cava	Sludge or no respiratory collapse and max diam. >2 cm
	Lungs	**No sliding and pulse, no B-lines, no consolidation
Cardiogenic	Heart	Hypokinetic left ventricle
	Lungs	**B pattern
Mixed	Pattern where criteria for more than a single diagnosis are satisfied (other than Hypovolemic/Distributive)	
Indefinite	Pattern where criteria for a single diagnosis are not satisfied or uncertain	

LV=Left Ventricle; RV=Right Ventricle; * At least two of these signs; **Necessarily present.

Table 3: The final charted hospital diagnoses of 108 cases complaining of symptomatic undifferentiated hypotension at presentation.

Hospital diagnosis	n	(%)
Sepsis (lung)	*25*	*(23.1)*
Sepsis (neoplasia progression)	*10*	*(9.2)*
Sepsis (urinary)	*10*	*(9.2)*
Dehydration	*9*	*(8.3)*
Sepsis (abdomen)	*8*	*(7.4)*
Pulmonary thromboembolism	*8*	*(7.4)*
Acute coronary syndrome	*7*	*(6.5)*
Cachexia	*7*	*(6.5)*
Acute heart failure	*6*	*(5.6)*
Sepsis (unknown)	*5*	*(4.6)*
Pericardial tamponade	*4*	*(3.7)*
Shock of unknown origin	*3*	*(2.8)*
Hypotensive pulmonary edema	*2*	*(1.8)*
Sepsis (skin)	*2*	*(1.8)*
Severe anemia	*1*	*(0.9)*
Hemoperitoneum	*1*	*(0.9)*

Table 4: Final clinical diagnoses based on chart assessment by three expert clinicians and ultrasonography diagnoses obtained at presentation in 108 patients with undifferentiated hypotension.

	Cardiogenic	Hypovolemic	Distributive	Cardiac Tamponade	Pulmonary Embolism	Hypovolemic/ Distributive	Mixed (other)	Indefinite
Clinical Diagnoses	10	12	40	3	6	18	6	13
Ultrasonography Diagnoses	15	11	35	3	8	21	8	7

Table 5: Statistic analyses comparing data of preliminary ultrasound diagnoses in patients with undifferentiated hypotension, with final clinical diagnoses. Analysis 1: the ultrasonography *hypovolemic/distributive* pattern was considered concordant with the clinical diagnosis *hypovolemic*, *distributive* and *mixed hypovolemic/distributive*. Analysis 2: the same as analysis 1, but in case of a *mixed* clinical diagnosis the ultrasonography pattern was considered concordant when the same of at least one of the two components. Analysis 3: the same as analysis 2, but performed by excluding the 13 cases with *indefinite* final clinical diagnosis.

	Number of cases	***Cohen k***	***95% CI***	***P***	***Ra***
Analysis 1	108	0.710	[0.614-0.806]	< 0.0001	0.768
Analysis 2	108	0.838	[0.761-0.914]	< 0.0001	0.870
Analysis 3	92	0.971	[0.932-1.000]	< 0.0001	0.978

CI = Confidence Intervals; P = p value; Ra = Raw agreement index.