ORIGINAL ARTICLE

Usefulness of Cardiac Index to Predict Early and 30-Day Mortality in Non-Cardiac Patients Being Admitted to Intensive Care Units

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ABSTRACT

Introduction: Cardiac index is a hemodynamic parameter defined as the ratio of the cardiac output, i.e., the volume of blood ejected from the left ventricle in 1 min, to the body surface area. This study aimed to assess the cardiac index to predict early and 30-day outcomes of non-cardiac patients being admitted to intensive care units using a non-invasive approach. **Materials and Methods:** This prospective cohort study included 31 non-cardiac patients who were consecutively admitted to the intensive care units of Rasoul-e-Akram Hospital, Tehran, Iran, in 2016. On admission, the simplified acute physiology score II to predict mortality and the cardiac output (by two-dimensional echocardiography) of each patient were determined. The cardiac index was calculated by dividing the cardiac output by the body surface area. In-hospital mortality and complications were assessed, and the association between simplified acute physiology score II and cardiac index was determined. The patients were followed-up 30 days after discharge by telephone to determine late death, occurrence of myocardial infarction, readmission, or re-hospitalization. **Results:** The mean cardiac index was significantly lower among the patients who died in intensive care units than in those who survived (2.86 ± 0.63 versus 3.70 ± 0.49, p = 0.006). A significant inverse association was found between Simplified Acute Physiology Score II and cardiac index (r = −0.539, p = 0.002). The length of hospital and intensive care units stay was not associated with Simplified Acute Physiology Score -II or cardiac index. The receiver operating characteristic curve analysis revealed that the cardiac index was effective in predicting in intensive care units mortality (area under curve = 0.857, p = 0.007). The best cut-off value for the cardiac index to predict in intensive care units mortality was 3.35, yielding a sensitivity of 83.3% and a specificity of 80.0%. **Conclusion:** Measuring the cardiac index during intensive care units admission using a noninvasive approach even in non-cardiac patients can predict in intensive care units mortality with high sensitivity and specificity.

INTRODUCTION

Cardiac index (CI) is a hemodynamic parameter defined as the ratio of the cardiac output, i.e., the volume of blood ejected from the left ventricle in 1 min, to the body surface area (BSA). It is a useful indicator of how well the heart is functioning as a pump (4) and is directly related to some cardiac characteristics, such as the power of heart performance, myocardial contractility, and cardiac size; thus, it tends to vary between individuals (1,2). The CI is usually assessed in critically ill patients to determine their cardiac function. Thermo-dilution via pulmonary artery catheter is a gold standard technique to measure the cardiac output (3). The CI is also considered as an important physiological and metabolic indicator of the metabolic status of various organs because the cardiac output is closely associated with the metabolic health of the organs (5,6). The cardiac function as a pump deteriorates due to several factors such as excessive weight and intraventricular conduction disorders in patients with acute coronary syndrome (7, 8).

Thus, it can be expected that the CI is considerably reduced in patients with functional impairment of vital organs, such as heart failure patients, critically ill patients, or those with metabolic disturbances. In addition, because many patients do not complete follow-up so refuse to undergo invasive procedures, CI assessment via noninvasive approaches will be valuable for determining the degree of cardiac performance or metabolic dysfunction (9).

Hence, the present study aimed to assess the CI to predict early and 30-day outcomes of non-cardiac patients being admitted to intensive care units (ICUs) using a noninvasive approach.

MATERIALS AND METHODS

This prospective cohort study included 31 non-cardiac patients who were consecutively admitted to the ICUs of

Rasoul-e-Akram Hospital, Tehran, Iran, in 2016. The study was approved by the ethics committee of Iran University of Medical Sciences and was conducted in accordance with the 1975 Declaration of Helsinki. Written informed consent was obtained from each patient prior to enrollment in this study. On admission to ICUs, the simplified acute physiology score (SAPS) II index of all patients was determined to predict their hospital mortality. Further, the cardiac output, left ventricular ejection fraction, and other cardiac functional parameters of all patients also determined by two-dimensional echocardiography by a single cardiologist. The CI was calculated by dividing the cardiac output by the BSA, which was calculated using the following formula provided by Kelley et al. (10) for measuring the BSA of female swine: BSA (m^2) = $0.0734 \times$ Weight $(kg)^{0.656}$. In-hospital mortality and complications, including increased troponin levels, serum creatinine levels, prolonged intubation, and other cardiac complications, were also assessed. To determine the long-term outcomes, the patients were followed-up 30 days after discharge by telephone to determine late death, occurrence of myocardial infarction, readmission, or re-hospitalization.

The results are presented as the mean ± standard deviation (SD) for quantitative variables and as absolute frequencies and percentages for categorical variables. Normality of the data was analyzed using the Kolmogorov–Smirnoff test. Quantitative variables were compared using the t-test or Mann–Whitney U test. The correlation between the study parameters was assessed using the Pearson's correlation test. The predicting power of the CI for discriminating between survived and non-survived patients was assessed using the area under the receiver operating characteristic (ROC) curve/area under curve (AUC) analysis. The ROC curve represents the ability of a parameter to discriminate between the true and false statuses in the same patient (11). The SPSS version 16.0 statistical software for Windows (SPSS Inc., Chicago, IL) was used for the statistical analyses. P values of ≤0.05 were considered statistically significant.

RESULTS

The baseline characteristics of the study patients are summarized in Table 1. Thirty-one patients with the mean age of 64.97 ± 16.88 (range, 19–84) years and the mean body mass index (BMI) of 27.16 ± 2.24 kg/m^2 were included, 58.1% of whom were male. The most frequent cardiovascular risk factors were smoking (35.5%), followed by hypertension (22.6%). Overall, one-third of the patients had left ventricular ejection fraction of 0.50. Twenty-one patients were directly admitted to the ICUs, whereas the others were transferred from the general ward to the ICUs. The main indications for ICU admission were gastric cancer (one case), pulmonary adenocarcinoma (one case), huge ascites (one case), chronic obstructive pulmonary disease exacerbation (one case), diabetic ketoacidosis (one case), post-esophagostomy (one case), gastrointestinal bleeding with pneumonia (one case), glioma symptoms (one case), hospital-acquired pneumonia(one case), metastatic

Table 1. Baseline characteristics of study population

| Variable	Descriptive statistics
Age (Mean)	64.97 ± 16.88
BMI (Mean)	27.16 ± 2.24
Pao2, mmHg (Mean)	65.26 ± 28.58
Fio2, mmHg (Mean)	49.39 ± 9.54
24h-urinary volume, mL (Mean)	2200.00 ± 1037.22
GCS Score (Mean)	8.06 ± 3.77
Male Gender (%)	58.1
History Of Cerebrovascular Disorders (%)	19.4
History Of Diabetes (%)	19.4
History Of Dyslipidemia (%)	3.2
History Of Hypertension (%)	22.6
History Of Cigarette Smoking (%)	35.5
History Of Opium Use (%)	12.9
Left Ventricular Ejection Fraction of 0.50 (%)	32.3%
Left Ventricular Ejection Fraction of 0.55 (%)	41.9%
Left Ventricular Ejection Fraction of 0.60 (%)	25.8%
Needing mechanical ventilation (%)	93.5%

(Abbreviations; BMI: Body Mass Index, Pao2: , Fio2: , GCS:)

ovarian cancer (one case), peritonitis (one case), aspiration pneumonia (seven cases), pneumosepsis (six cases), primary sepsis (four cases), shunt-related infection (one case), thyroid cancer (one case), and trauma (one case). The mean length of ICU stay was 26.60 ± 36.68 (range, 2–133) days. The most common in-ICU complications were related to thromboembolic events (13.0%), renal failure (45.2%), cardiac arrhythmias (29.0%), cardiac arrest (58.1%), and various infections (80.6%). The mean length of complete hospital stay was 34.61 ± 36.48 (range, 2–133) days. The in-ICU mortality rate was 80.6%.The 30-day post-discharge follow-up revealed that one patient had died within 25 days after hospital discharge; this increased the 30-day mortality rate to 86.7%. This follow-up also revealed that two patients were re-hospitalized.

The mean SAPS II was 52.39 ± 14.45 (range, 21–89), and the mean CI was 3.03 ± 0.69 (range, 0.80–4.20). The mean SAPS II was significantly higher in the in-ICU non-survived group than in the survived group (54.36 ± 13.85 versus 44.17 ± 15.20, p = 0.002). In addition, the mean CI was significantly lower in the in-ICU non-survived group than in the survived group (2.86 ± 0.63 versus 3.70 ± 0.49, p = 0.006). These results indicated a significant inverse correlation between SAPS-II and CI (r = −0.539, r^2 = 0.291, p = 0.002) (Figure 1). Further, among patients with SAPSII <40, all had CI ≥ 3, whereas among those with SAPS II > 40, only 44.0% had CI > 3.These findings confirmed the significant inverse association between SAPSII and CI. The length of ICU stay was not associated with SAPS II (r^2 = 0.001, p = 0.945) or CI (r = 0.075, r^2 = 0.006, p = 0.687). Similarly, the mean length of complete
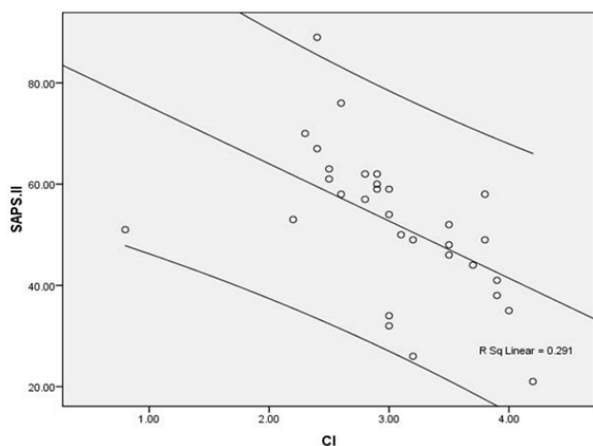
Figure 1. Reverse association between SAPS II and CI
(Abbreviations; SAPS II: simplified acute physiology score II, CI: cardiac index)
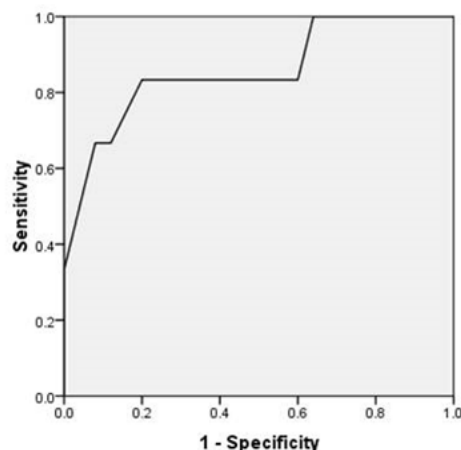
Figure 2. The ROC curve analysis to assess the value of CI to predict in-ICU mortality
(Abbreviations; ROC: receiver operating characteristic, CI: cardiac index, ICU: intensive care unit)

hospital stay was not associated with SAPS II ($r = -0.088$, $r^2 = 0.008$, $p = 0.637$) or CI ($r = 0.091$, $r^2 = 0.008$, $p = 0.625$). The ROC curve analysis (Figure 2) revealed that the CI could effectively predict the in-ICU mortality (AUC $= 0.857$, $p = 0.007$). The best cut-off value for the CI to predict in-ICU mortality was 3.35, yielding a sensitivity of 83.3% and a specificity of 80.0%.

DISCUSSION
The CI is a valuable parameter for estimating the cardiac performance in relation to the BSA. Although usually used to determine the cardiac output of critically ill patients, our results showed that it can also be valuable in predicting the outcome of patients being admitted to ICUs. In this study, we introduced CI as a valuable index for predicting mortality similar to SAPS II, a powerful indicator of in-ICU mortality among critically ill patients. In our patient cohort, a lower CI reflected a higher risk of in-ICU death, indicating that the CI could effectively discriminate between survived and non-survived conditions with high sensitivity and specificity. However, one death occurred during the first 30 days after discharge; therefore, we could not assess the value of CI to predict 30-day mortality. In addition, no significant association was found between the CI and the length of ICU or complete hospital stay, indicating that the CI cannot predict the duration of hospitalization.

Many studies have reported the power of CI to predict mortality in ICU patients. For example, in the study by Fincke et al. (12), CI was the only parameter used to predict in-hospital mortality of patients undergoing cardiogenic shock. However, only cardiac patients were assessed in their study. In another study by Soussi et al. (13), 30-day mortality was considerably lower (42.0%) than that in our study, indicating that the condition of our patients was worse. However, consistent with our results, the CI assessed during admission in their study could also effectively predict early mortality. In another study, Kimmoun et al. (14) assessed the CI during admission as well as 24 hours after admission. In their study, SAPS II

of>58 and CI were predictive of 30-day and in-hospital mortalities, consistent with our findings.

Several invasive techniques are available for CI assessment, including transpulmonary thermos-dilution technique, angiography, and impedance cardiography. However, their use has now decreased because of their invasive nature and their poor ability to determine the cardiac functional status. For instance, as indicated by Eiferman et al. (15) following the introduction of pulmonary artery catheter (PAC) and recognition of the importance of preload as a critical determinant of the cardiac function, various hemodynamic monitoring methods were developed to assess cardiac function parameters, such as cardiac output or cardiac index; however, the lack of concordance between these devices has been also revealed in critically ill patients. Because our study mainly aimed to determine the prognostic value of CI and our patients were reluctant to undergo invasive methods for measuring CI, we estimated the CI using a noninvasive approach, i.e., by dividing the cardiac output by the BSA as previously described (16,17). The present study had some limitations. First, the small sample size of the study could have resulted in inadequate power to determine between-parameter associations while considering potential confounding factors. Second, because the CI was not determined using invasive methods, measurement biases while measuring the cardiac output and BSA cannot be ruled out.

CONCLUSION
In conclusion, measuring the CI during ICU admission using a noninvasive approach even in non-cardiac patients can predict in-ICU mortality with high sensitivity and specificity. However, the CI cannot predict the length of hospital or ICU stay.

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of the project.

This study was approved by the ethics committee of Iran University of Medical Sciences. Informed consent was obtained from all patients or their families. Human rights were respected in accordance with the Helsinki Declaration.

AUTHER CONTRIBUTIONS
All authors contributed equally.

CONFLICT OF INTEREST
The authors have no conflict of interest and/or no funding to disclose.

ETHICAL STANDARDS
The study was approved by the ethics committee of Iran University of Medical Sciences and was conducted in accordance with the 1975 Declaration of Helsinki. Written informed consent was obtained from each patient prior to enrollment in this study.

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