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Original Contribution

E-point septal separation: a bedside tool for emergency physician assessment of left ventricular ejection fraction☆,☆☆,★

Conor J. McKaigney, MD [a,b,*], Mori J. Krantz, MD [c,d], Cherie L. La Rocque, MSc [e], Nicole D. Hurst, MD [b,f], Matthew S. Buchanan, MD [b,g], John L. Kendall, MD [b,g]

[a] Department of Emergency Medicine, Queen's University, Ontario, Canada
[b] Department of Emergency Medicine, Denver Health Medical Center, Denver, CO
[c] Division of Cardiology, Denver Health Medical Center, Denver, CO
[d] Department of Medicine, University of Colorado School of Medicine, Aurora, CO
[e] Department of Psychology, Queen's University, Ontario, Canada
[f] Naval Medical Center, San Diego, CA
[g] Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, CO

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ABSTRACT

Objectives: Rapid assessment of left ventricular ejection fraction (LVEF) may be critical among emergency department (ED) patients. This study examined the predictive relationship between ED physician performed bedside mitral-valve E-point septal separation (EPSS) measurements to the quantitative, calculated LVEF. We further evaluated the relationship between ED physician visual estimates of global cardiac function (GCF) and calculated LVEF values.

Methods: A prospective observational study was conducted on a sequential convenience sample of patients receiving comprehensive transthoracic echocardiography (TTE). Three ED ultrasound fellows performed bedside ultrasound examinations to obtain both EPSS measurements and subjective visual GCF estimates. A linear regression analysis was conducted to examine the relation of EPSS to the calculated LVEF from the comprehensive TTE. Agreement (modified Cohen κ) between ED ultrasound fellow GCF estimates and the calculated LVEF was also assessed.

Results: Linear regression analyses revealed a significant correlation ($r = 0.73$, $P < .001$) between bedside EPSS and the calculated LVEF. The sensitivity and specificity of an EPSS measurement of greater than 7 mm for severe systolic dysfunction (LVEF $\leq$30%) were 100.0% (95% confidence interval, 62.9-100.0) and 51.6% (95% confidence interval, 38.6-64.5), respectively. Subjective estimates of GCF were moderately correlated with calculated LVEF (Cohen $\kappa = 0.58$).

Conclusions: Measurements of EPSS by ED physicians were significantly associated with the calculated measurements of LVEF from comprehensive TTE. Subjective visual estimates of GCF, however, demonstrated only moderate agreement with the calculated LVEF. An EPSS measurement greater than 7 mm was uniformly sensitive at identifying patients with severely reduced LVEF.

1. Introduction

In 2010, the American Society of Echocardiography and the American College of Emergency Physicians released a joint consensus statement that advocated timely bedside echocardiography for the assessment of pericardial effusion, relative chamber size, and global cardiac function (GCF) [1]. Despite this consensus, the best approach to assess GCF in the emergency department (ED) setting has not been determined. Although most ED echocardiographic studies have used a quantitative calculated method to estimate left ventricular ejection fraction (LVEF), calculated measures are difficult to perform and time-consuming, which limits their use in the ED setting [2,3]. Most ED physicians are not trained in calculating quantitative estimates of LVEF but, rather, are accustomed to subjective visual assessments of cardiac function. There are only a limited number of studies that suggest visual estimates by ED physicians correlate with quantitative and semiquantitative methods of estimating GCF [4,5]. The major limitation of this visual or "eyeballing" method for evaluating LVEF is that it is observer dependent and engenders a great deal of subjectivity into the final estimate [6].

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* Corresponding author. Department of Emergency Medicine, Queen's University, Kingston, Ontario, Canada.
E-mail address: 9cjm1@queensu.ca (C.J. McKaigney).

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An alternate method for estimating LVEF is the mitral valve E-point septal separation (EPSS) [7]. In early diastole, the anterior leaflet of the mitral valve should approach or touch the interventricular septum in healthy individuals. This is the E-point of the mitral valve cycle. The amount of separation between the valve leaflet and the septum in early diastole is defined as the EPSS. Not only is it an index of left ventricular function and dilation, it also has a strong negative correlation with LVEF [8,9]. Specifically, a measurement of greater than 7 mm has been shown to predict poor left ventricular function [10].

One study in the ED literature examined EPSS as a measure of LVEF, demonstrating a correlation in a subset of patients with acute dyspnea [11]. These resident-performed EPSS measures were compared with the attending ED physicians' visual assessment of LVEF. This secondary assessment was made from stored video of the resident study. Although half of these bedside ultrasounds were also reviewed by cardiologists, the EPSS was not compared with the clinical standard for evaluation of LVEF in the ED, that being the formal or comprehensive echocardiogram, performed by trained sonographers and interpreted by board-certified noninvasive cardiologists.

Given this background, we sought to determine whether EPSS measurements obtained by ED physicians correlate with the calculated LVEF from comprehensive transthoracic echocardiography (TTE). We also investigated the use of an absolute EPSS value greater than 8 mm to identify subjects with any systolic dysfunction (defined as LVEF <55%) and 7 mm to predict severe systolic dysfunction (defined as LVEF <30%) Secondarily, we evaluated whether bedside visual estimates of GCF correlated with the same calculated LVEF measurements. Our hypothesis was that a stronger relationship with LVEF would be demonstrated using EPSS measurements compared with subjective estimates currently used by most ED physicians performing bedside cardiac ultrasonography.

2. Methods

2.1. Study design

This was a prospective observational study evaluating the relation of mitral valve EPSS to LVEF for unselected hospitalized patients undergoing comprehensive TTE for any indication. The study was approved by the state institutional review board.

2.2. Subjects

Eighty adult subjects were consecutively recruited as a convenience sample between February and April 2012 from an academic level I trauma center, with approximately 55 000 ED visits per year. Subjects were approached for enrollment and included if they presented through the ED and their treating physician had ordered TTE. Exclusion criteria were known pregnancy or age less than 18 years. Subjects were enrolled within 8 hours of their comprehensive TTE study. Seven (8.8%) subjects were enrolled in the ED, 11 (13.8%) in the intensive care unit, and the remaining 62 (77.5%) on the inpatient ward.

2.3. Measures

All bedside echocardiographic examinations were completed using a Logic P6 ultrasound unit with a 2.5 MHz (1.8-3.5) phased-array transducer (General Electric, Fairfield, CT). Comprehensive TTE was performed with an iE33 echocardiography system (Phillips, Andover, MA), and cardiologist interpretation was completed on a digital workstation (Phillips Xcelera, the Netherlands). Investigators were 3 emergency ultrasound fellows (7 months into a 1-year fellowship), who had each completed more than 100 bedside echocardiograms prior to commencement of the study. All investigators had received training in both visual and calculated LVEF estimation as part of their fellowship. Furthermore, they received a 10-minute didactic presentation on EPSS and had 3 separate supervised EPSS measurements with the principal investigator.

Demographic (age, sex), physical examination, and measurement data were collected at the point of service. Physical examination data included heart rate, respiratory rate, systolic and diastolic blood pressures, and weight. Ultrasound data included subjective estimates of GCF using a 3-category ordinal scale (good, moderately reduced, poor) and EPSS measurements.

2.4. Study protocol

Within 24 hours of comprehensive echocardiography, ED investigators, blinded to the TTE results, performed a bedside 4-view basic echocardiographic examination, consisting of subxiphoid, parasternal long, and parasternal short and apical views. Based on the 4 views, categorical subjective estimates of GCF were made. These categories were defined as normal systolic function (LVEF >55%), moderate systolic dysfunction (30% > LVEF > 55%), and severe systolic dysfunction (LVEF <30%), according to visual estimation of the radial change in left ventricular chamber size from diastole to systole [12]. After the subjective estimates of GCF were recorded, the investigators obtained a separate parasternal long-axis view where M-mode measurements of the EPSS were performed. Measurements were taken in early diastole as the smallest distance (in millimeters) between the tip of the anterior mitral valve leaflet and the interventricular septum (Fig. 1). To determine interrater reliability, 30% of the study population (23 patients) was randomly selected to have a second bedside ultrasound study performed independently by another investigator, blinded to the results of the first examination.

Comprehensive TTE was separately performed by certified cardiac ultrasonographers who were unaware of the current study. Calculated measurements of LVEF were made using the Teichholz method, which involves an algorithm derived from linear chamber measurements between systole and diastole in the parasternal view using M-Mode [13,14]. These measurements were subsequently categorized to match the ranges used for estimates of GCF: normal systolic function (LVEF >55%), moderate systolic dysfunction (30% > LVEF > 55%), or severe systolic dysfunction (LVEF <30%).

2.5. Data analysis

Statistical analyses were performed using SPSS statistical software Version 19 (IBM, Armonk, NY). A linear regression analysis was conducted to examine the relation of EPSS to the calculated Teichholz LVEF. This calculated LVEF value was specified in order to facilitate the comparison of continuous variables. Time from initial comprehensive TTE to bedside EPSS measurements (study interval time; in minutes) was controlled for in the first step of the regression model, along with any demographic or physical examination variables that were found to be significantly related to the main test variables (ie, EPSS and LVEF). Calculated LVEF measurements were entered in the second step of each model. Multicollinearity was assessed by examining variance inflation factor values for each predictor variable and bivariate relations among these variables. Variance inflation factor values of less than 5 and bivariate correlations of small to medium ($|\text{Pearson } r\text{'s}| = 0.1\text{-}0.5$) magnitude were assumed to indicate the absence of high multicollinearity [15,16]. Sensitivity and specificity of EPSS measurements in predicting severely systolic dysfunction (LVEF <30%) were calculated using the criterion of an abnormal EPSS greater than or equal to 7 mm. Sensitivity and specificity of EPSS measurements in predicting any systolic dysfunction (defined as LVEF <55%) were calculated using the criterion of an abnormal EPSS greater than or equal to 8 mm. Our cutoff values of 7 mm for severe systolic dysfunction and 8 mm for any systolic

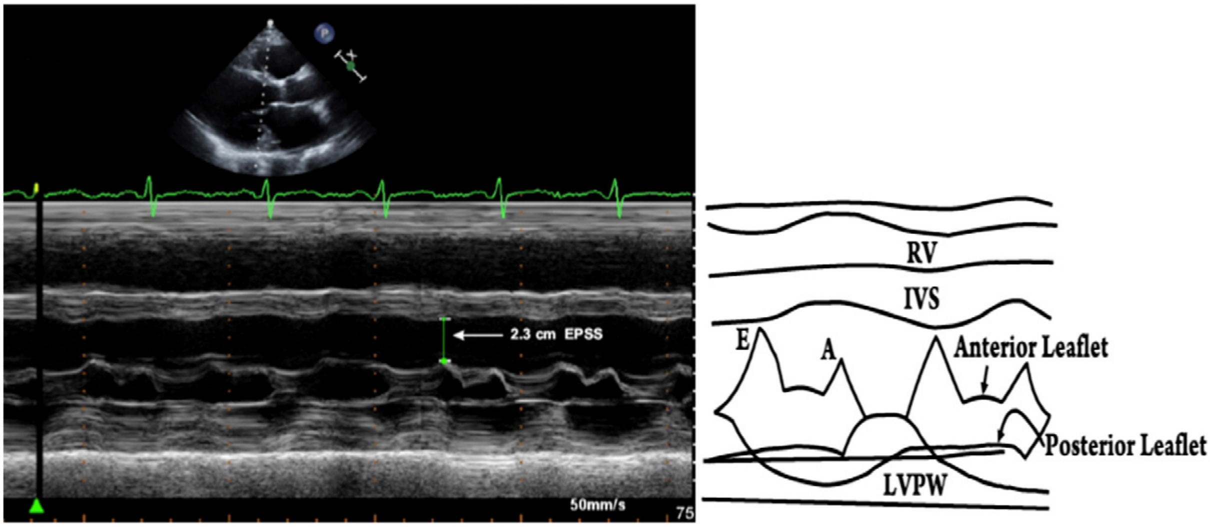

Fig. 1. Parasternal long-axis view of the heart in the setting of severe left ventricular systolic dysfunction. The upper panel depicts the 2-dimensional parasternal long-axis view. In the M-mode view, a cursor is used at the level of the anterior leaflet of the mitral valve to determine the smallest distance between the septum and the valve, which represents the EPSS. The drawing on the right corresponds to the M-mode tracing. E-point is the peak excursion of the anterior mitral leaflet during passive left ventricular filling. The A-point represents anterior leaflet excursion during atrial systole. LVPW, left ventricular posterior wall; IVS, interventricular septum; RV, right ventricle.

dysfunction were chosen a priori based on previous parameters described in the EPSS literature [7,11,17].

Visual analyses were conducted to examine agreement (modified Cohen κ) between the ED physicians' categorical GCF estimates and the calculated LVEF. Interobserver agreement was also computed for investigators' GCF estimates (modified Cohen κ) and EPSS measurement (Spearman r value), respectively.

3. Results

The sex distribution of participants in the cohort was 63.7% (n = 51) male and 36.3% female (n = 29). Other pertinent demographic data are depicted in Table. For regression analyses, 8 subjects without a calculated LVEF and 1 participant without an EPSS measurement were excluded, resulting in a sample of 71 unique individuals. The same cohort was available for categorical analyses.

Calculated LVEF ranged from 13% to 86% ($M = 55.42$, SD = 17.51) and EPSS ranged from 0.50 to 29.70 mm ($M = 9.33$, SD = 6.91). Both EPSS and LVEF estimates differed significantly across sex, with men having higher EPSS scores than women (in millimeters) ($t_{71.99} = 3.47$, $P = .001$; $M = 11.08$ [SD = 7.68] vs $M = 6.39$ [SD = 4.00]), as well as higher calculated estimates of LVEF [$M = 63.64$ [SD = 11.44] vs $M = 50.56$ [SD = 18.73]; $t_{67.89} = -3.63$, $P < .001$). Because these quantitative estimates differed significantly for men and women, sex was entered in the regression model as a potential covariate. No other demographic or clinical variables were significantly associated with LVEF or EPSS estimates. In the linear regression model, EPSS emerged as a statistically significant predictor ($P < .001$) of calculated LVEF. This resulted in a regression equation of LVEF = 71.25 − 1.67 · EPSS (mm) and a correlation of $r = 0.73$ ($0.60 \leq$ 95% confidence interval [CI_{95}] ≤ 0.82), as depicted in Fig. 2. Multicollinearity did not emerge as a confounder (all variance inflation factor values <1.14; all |Pearson r's| ≤ 0.34). The sensitivity and specificity of an EPSS measurement of greater than 7 mm for severely reduced LVEF were 100.0% (95% CI, 62.9-100.0) and 51.6% (95% CI, 38.6-64.5), respectively. The corresponding positive likelihood ratio was 2.07, and the negative likelihood ratio was 0.00. The sensitivity and specificity of an EPSS measurement of greater than 8 mm for any systolic dysfunction were 83.3% (95% CI, 62.6-95.2) and 50.0% (95% CI, 29.2-70.9), respectively. The corresponding positive likelihood ratio was 1.67, and the negative likelihood ratio was 0.33.

The percentages of subjects classified by calculated LVEF as normal, moderately reduced, and severely reduced systolic function were 57.7 (n = 41), 32.0 (n = 22), and 11.3 (n = 8), respectively. The percentages of subjects subjective estimates classified as normal GCF, moderately reduced GCF, and poor GCF were 51.9 (n = 40), 24.7 (n =

Table
Demographic and physical examination variables

	Mean	SD	Range
Age (y)	58.0	15.1	22-100
Heart rate (beats/min)	81.0	14.9	12-126
Respiratory rate (breaths/min)	16.9	2.7	12-26
Systolic blood pressure (mm Hg)	127.1	21.2	93-189
Diastolic blood pressure (mm Hg)	73.2	14.1	23-117
Weight (kg)	84.9	24.9	43-115
Study interval time (min)	360	474	11-1620

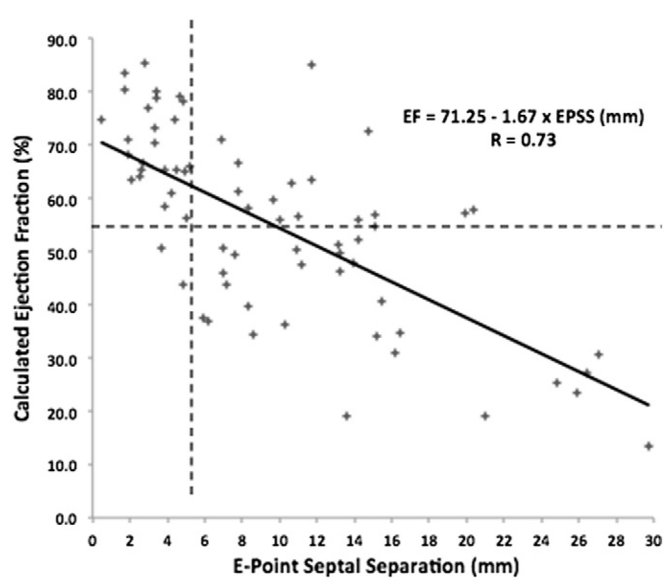

Fig. 2. Scatterplot of linear regression for calculated LVEF vs EPSS. Vertical (hashed) line represents the 7-mm cutoff point for EPSS, and horizontal (hashed) line represents the cut point for LVEF greater than 55.0%.

19), and 23.4 (n = 18), respectively. When these categorical estimates (LVEF vs GCF) were compared, raw agreement was seen in only 49 subjects (69.0%), resulting in a weighted Cohen κ of 0.58. The strongest agreement (100%) was found for subjects with severe systolic dysfunction (n = 8). In subjects with any systolic dysfunction (n = 10), agreement was seen 45.5% of the time, and in those with normal systolic function (n = 31), agreement was seen 75.6% of the time. Interobserver correlation for EPSS measurements suggested a high level of agreement (Spearman $r = 0.87$; $P < .01$). Interobserver GCF estimates resulted in a κ of 0.49, suggesting moderate correlation.

4. Discussion

This study demonstrates that EPSS measurements performed by ED physicians are strongly correlated with calculated LVEF assessments obtained by comprehensive TTE. Moreover, contrary to prior literature, our results suggest that even with advanced bedside ultrasound training, emergency physicians are not as proficient at subjective visual estimation of systolic function as previously described [4,5]. This highlights the potential importance of a reliable point-of-service predictor for ED interpretation of left ventricular systolic function, which could augment information obtained from visual inspection.

The EPSS is an easily obtained value taken from the parasternal long-axis view with the patient in a supine or semirecumbent position. It can be acquired rapidly and requires only a single linear distance measurement with onscreen digital calipers. It has been shown to reflect the net effect of cardiac motion throughout the entire ventricle and requires no assumptions regarding ventricular shape [17]. Our results show that the EPSS can be obtained consistently, with strong interobserver agreement, which was not achieved using visual estimates of GCF. Beyond requiring only a single view of the heart, EPSS requires very little active patient cooperation and positioning. With other views, subject movement into the lateral decubitus position is often necessary to adequately visualize the heart. The apical 4-chamber view, for example, is often obscured by body habitus and lung pathology in the supine position. In our subjects, the parasternal long view was reliably obtained, likely because it was influenced less by these patient level factors. This is consistent with prior research, which has shown that the parasternal long-axis view is preferred for emergent bedside echocardiography [18].

Our bedside EPSS measurements were strongly correlated with the calculated LVEF from the comprehensive TTE. This is the first ED study suggesting that a modest regression equation based on the EPSS can provide a quantitative estimate of the LVEF. A recent ED study by Weekes et al [19] demonstrated a moderate negative correlation between ED physician–performed EPSS measurements and fractional shortening measurements of LVEF. Their study did not, however, demonstrate that EPSS predicts LVEF using linear regression, an additional finding that extends the evidence for EPSS assessment in the ED.

Our results agree with those from Secko et al [11], which similarly showed a strong correlation between EPSS and LVEF, performed on a subset of patients with dyspnea. Our study differs in a variety of important ways. First, the subjects in our study were ED patients whose physicians had ordered a TTE, regardless of indication, adding generalizability to the findings, because determination of systolic function in the ED is needed to address a broader spectrum of clinical indications. Second, all comprehensive echocardiograms were independently performed and reviewed. In addition, EPSS measurements were compared directly to the calculated LVEF from comprehensive TTE examinations. This contrasts with the study of Secko et al, which involved ED physicians and cardiologists estimating LVEF based on video obtained by the residents performing the study. Comparing the EPSS with comprehensive TTE better characterizes the relationship between the clinical standard for determining LVEF and those obtained at the point-of-service among ED patients.

It is noteworthy that the visual estimates of GCF had only moderate agreement when compared with the calculated values. These results are in contrast to the 86.1% overall agreement seen by Randazzo et al [4] between cardiologist- and ED physician–performed visual estimates of LVEF. It is possible that our results may have been influenced by a skewed distribution of systolic function because most of our subjects fell into the category of normal systolic function. Of the small number of subjects with severe systolic dysfunction, we were able to achieve the strongest agreement.

Interestingly, an EPSS greater than 8 mm appears to be fairly sensitive at predicting any systolic dysfunction. This may be important in the early diagnosis of patients with asymptomatic left ventricular systolic dysfunction. A more established cut point in the ED literature is the use of an EPSS of greater than 7 mm to determine those patients with severe systolic dysfunction [10]. In our study, this had 100% sensitivity for identifying patients with an LVEF less than 30%. A recent single-center study evaluated the combination of LVEF estimation, collapsibility index of the inferior vena cava, and assessment of the pleura for presence of B-lines to predict a final adjudicated diagnosis of acute decompensated heart failure. The combination of these measures dramatically increased the specificity of diagnosis and could inform future studies that include EPSS measurement [20].

5. Limitations

The current study has a number of inherent limitations. The EPSS value may be unreliable in certain pathologic states, which can lead to both underestimations and overestimations of the LVEF. Specifically, mitral valve stenosis can lead to overestimation of the EPSS and subsequent underestimation of LVEF, although in the current study, none of the subjects had mitral stenosis. Moreover, with diminishing incidence of rheumatic fever in the developed world, mitral stenosis is substantially less prevalent and unlikely to impact ED assessment of EPSS [21]. We did not make an attempt to exclude patients with valvular disease, atrial fibrillation, or bundle branch block in order to enhance generalizability.

In using the Teichholz method, there are inherent inaccuracies that result from the geometric assumptions required to convert a linear measurement to a 3-dimensional volume. The geometric assumptions are limited mostly when there is apical dyskinesis or akinesis. However, in our cohort, there was not a high background of patients with obstructive coronary artery disease, so the assumptions are likely to be reasonable.

Data collection was based on convenience sampling. Although this should have no role on the correlation of the EPSS measurements with LVEF, our primary study objective, it may have increased the time interval between the comprehensive TTE and the bedside examinations. The mean time between the study examination and the comprehensive echocardiogram was approximately 6 hours. Although unlikely, it is theoretically possible that systolic function may have changed in this interval because of alterations in physiologic state such as acidosis, sepsis, or use of vasopressors. An attempt was made, however, to account for this during the regression analysis in which the interval time between ultrasound examinations did not emerge as a significant covariate. Although all patients presented through the ED, few patients received their study within the ED itself. This was due to a policy of rapid patient transition to the ward in our hospital to avoid diverting patients to another institution. Nonetheless, the absence of multiple exclusion criteria suggests that the study cohort was representative of our typical ED population.

The small number of patients with severely reduced LVEF is an important study limitation; a larger study may have allowed us to include a greater number of patients with severe systolic dysfunction. Finally, only emergency ultrasound fellows performed the examinations. Although this may limit the ease of adoption of EPSS, junior residents have previously been shown to successfully obtain EPSS measurements with only limited training [11]. Finally, a formal sample size calculation was not conducted owing to the paucity of the literature, although our study was likely underpowered to detect small differences in performance characteristics among methods to assess the LVEF.

6. Conclusions

Our study suggests that ED physicians are able to rapidly assess left ventricular systolic function using the mitral valve EPSS and that it is strongly correlated with calculated LVEF. A prediction of LVEF from a linear regression equation using EPSS measurements could theoretically be used to generate a quantitative prediction of LVEF. An EPSS greater than 7 mm may be used to predict patients with severely reduced LVEF. In contrast to prior literature, ED physician visual estimation of systolic function did not perform as well in our study. The association between EPSS and LVEF in our regression model adds to the small but growing volume of literature on ED physician–performed EPSS measurements. A larger, multicenter study, however, would be required to compare the use of EPSS and visual estimation of systolic function. In the era of comparative effectiveness research, a future prospective study to assess the impact of EPSS obtained in the ED on the quality and appropriateness of downstream inpatient care seems warranted.

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