Autonomic Nervous System Activity as Risk Predictor in the Medical Emergency Department: A Prospective Cohort Study

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Objectives: To evaluate heart rate deceleration capacity, an electrocardiogram-based marker of autonomic nervous system activity, as risk predictor in a medical emergency department and to test its incremental predictive value to the modified early warning score.

Design: Prospective cohort study.

Setting: Medical emergency department of a large university hospital.

Patients: Five thousand seven hundred thirty consecutive patients of either sex in sinus rhythm, who were admitted to the medical emergency department of the University of Tübingen, Germany, between November 2010 and March 2012.

Interventions: None.

Measurements and Main Results: Deceleration capacity of heart rate was calculated within the first minutes after emergency department admission. The modified early warning score was assessed from respiratory rate, heart rate, systolic blood pressure, body temperature, and level of consciousness as previously described. Primary endpoint was intrahospital mortality; secondary endpoints included transfer to the ICU as well as 30-day and 180-day mortality. One hundred forty-two patients (2.5%) reached the primary endpoint. Deceleration capacity was highly significantly lower in nonsurvivors than survivors (2.9 ± 2.1 ms vs 5.6 ± 2.9 ms; $p < 0.001$) and yielded an area under the receiver-operator characteristic curve of 0.780 (95% CI, 0.745–0.813). The modified early warning score model yielded an area under the receiver-operator characteristic curve of 0.706 (0.667–0.750). Implementing deceleration capacity into the modified early warning score model led to a highly significant increase of the area under the receiver-operator characteristic curve to 0.804 (0.770–0.835; $p < 0.001$ for difference). Deceleration capacity was also a highly significant predictor of 30-day and 180-day mortality as well as transfer to the ICU.

Conclusions: Deceleration capacity is a strong and independent predictor of short-term mortality among patients admitted to a medical emergency department. (*Crit Care Med* 2015; 43:1079–1086)

Key Words: cardiac autonomic function; electrocardiogram; emergency department; heart rate variability; risk stratification

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Drs. Eick and Bauer developed the technology. Dr. Rizas did the statistical analyses. Drs. Eick, Rizas, and Bauer designed the study. Drs. Zürn and Groga-Bada organized the follow-up of the patients. Dr. Hamm critically revised the study. Drs. Kreth, Overkamp, and Weyrich were involved in patient enrollment. Dr. Gawaz helped to design the study. Dr. Bauer wrote the report with input from all other authors.

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In most healthcare systems around the world, emergency departments (EDs) are the frontline venue to provide acute medical treatment. However, deficits in ambulatory care, demographic changes, and the rising complexity of diseases led to a dramatic increase in the number of admissions over the past years (1, 2). So-called ED overcrowding became a serious healthcare problem directly affecting the quality of patient care and mortality (3, 4). A recent population-based study showed an increase of intrahospital mortality by 79% when waiting times exceeded 6 hours (5).

Rapid risk stratification at first contact to define appropriate treatment priorities is of key importance to overcome limited resources. Current concepts of initial risk stratification are

based on clinical judgment, vital signs, including respiratory rate, heart rate, arterial blood pressure (BP), and body temperature, and neurological status. For clinical practice, these variables can be combined using a multivariable scoring system such as the "modified early warning score" (MEWS) (6–8). The MEWS can be quickly assessed within minutes by nursing staff before completion of any laboratory or other diagnostic tests. However, although the MEWS has been shown to significantly predict adverse events, it lacks both sensitivity and specificity for clinical decision making. Therefore, complementary approaches for risk stratification at first contact are of great clinical interest.

Essential information about the current condition of a patient can be derived from the functional status of the autonomic nervous system (ANS). The ANS is an integrated neural network connecting all vital organ systems. Severe damage of any organ within the network leads to a global change in the functional status of the ANS. Analyzing autonomic modulations of the sinus node by means of heart rate variability (HRV) has practical appeal as beat-to-beat intervals can be obtained noninvasively by a routine electrocardiogram (ECG) (9). Over the last decades, numerous measures have been proposed to assess HRV including standard measures in time and frequency domains (9) as well as complexity measures such as sample entropy (SampEN) or the multiscale sample entropy (MSE) index (10–13). Previous studies indicated that a depressed HRV has prognostic implications in various diseases, including myocardial infarction (14), heart failure (15), sepsis (16, 17), pulmonary diseases (18), stroke (19), hemorrhagic shock (20), renal failure (21), and trauma patients (22).

However, automated and reliable assessment of HRV in the setting of an ED is limited by the huge amount of noise and nonstationarities in ECG signals obtained under routine clinical conditions. Phase-rectified signal averaging (PRSA) is a robust signal processing algorithm that is capable of extracting periodic components out of noisy ECG signals. In previous studies, PRSA-based deceleration capacity (DC) of heart rate has been shown to yield strong and independent prognostic information in survivors of acute myocardial infarction (23, 24). DC is an integral measure of all deceleration-related oscillations of heart rate and considered to be a measure of overall tonic autonomic activity. Recently, we presented a refinement of the technology, including optimized R-peak detection and filtering techniques, allowing for a fully automated assessment of DC from unprocessed noisy ECG signals (25).

In the present study, we tested the prognostic power of DC in prediction of intrahospital mortality among patients admitted to a medical ED and compared it to standard and complexity measures of HRV. Furthermore, we aimed to assess the incremental value of DC to the MEWS model. We hypothesized that impaired DC was a strong and independent predictor of intrahospital mortality and that implementing DC into the MEWS model improved the predictive power of the MEWS model alone.

MATERIALS AND METHODS

Participants

Consecutive patients of either sex were prospectively enrolled between November 2010 and December 2012 if they were admitted to the medical ED of the University of Tübingen, Germany. Patients were included if they were 18 years old or older and presented in sinus rhythm, which is required for the assessment of cardiac autonomic function. **Figure 1** shows the flowchart of the validation cohort. The study was approved by the local ethics committee.

Biosignal Recording

The ED was equipped with six monitoring devices (DASH 4000/5000 and Teleguard, General Electrics, Fairfield, CT; sample frequency, 100 Hz). Nursing staff were advised to monitor patients directly after admission. Treating physicians were blinded to the study design. Management of patients in the ED was not influenced by monitoring. In particular, monitoring did not delay any diagnostic or therapeutic procedures.

Assessment of DC

Technical details of the methodology of automated assessment of DC have been described elsewhere (25). To account for the substantial noise and artifacts in the absence of manual editing, extensive filtering techniques and transformations were applied to the ECG raw signals to obtain the sequence of RR intervals. Briefly, a band-pass filter (4th order Chebyshev bandwidth filter 6–18 Hz) was applied to the signal followed by a 1st order forward differencing filter. Amplitudes were normalized and nonlinearly transformed using the Shannon energy envelope. Subsequently, a Hilbert

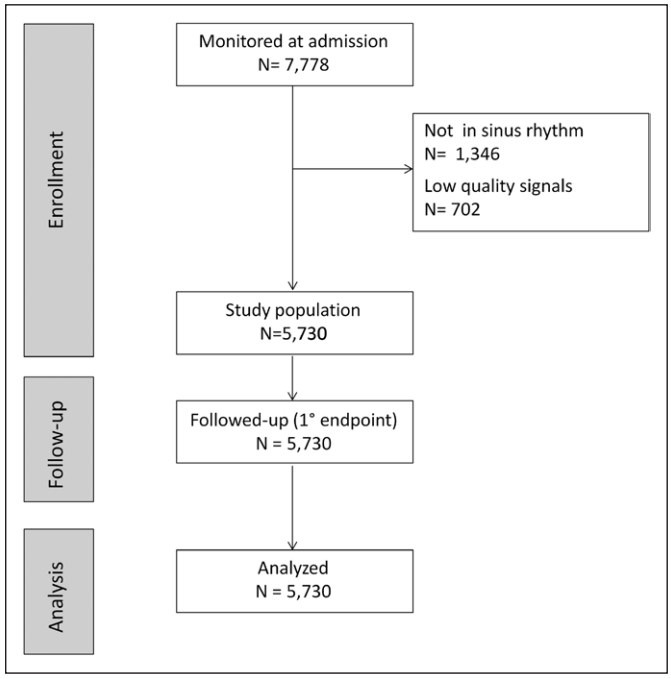

Figure 1. Enrollment, follow-up, and analysis of the study.

transformation and a moving average filter (250 samples) were applied followed by a Savitzky-Golay filter (frame 15, degree 0). Times of zero-crossing were identified and the R-peaks were searched.

The first 10 minutes of the recordings were used for DC computation. In case of low signal quality, the time frame was gradually extended to a maximum of 30 minutes until at least 200 anchors suitable for DC computation (see below) were detected. This led to an average recording time of 14.3 ± 8.5 minutes.

The RR time series were checked for the presence of atrial fibrillation using a validated automated algorithm (26). Recordings with atrial fibrillation were excluded from further analysis. The RR time series were transformed by PRSA (27) to obtain a modified, more robust version of DC (23). DC is an integral measure of the periodic power of all deceleration-related oscillations of heart rate in the observation period. The exact methodologies of PRSA and DC assessment have been described elsewhere (27). Briefly, instances within the RR interval time series are identified where the heart rate decelerates (so-called anchors). The central part of the PRSA signal is then quantified by Haar wavelet analysis to obtain an estimate of DC. The PRSA technology allows for several adjustments, which make the method more robust to artifacts and noise and improve agreement between automatically and manually processed ECGs (25). Here, we used $T = 4$ (instead of 1; equation 2a in [27]) and $s = 5$ (instead of 2; equation 8 in [27]). **Figure 2** exemplarily shows the phase-rectified signal of a patient who survived the hospital stay (**Fig. 2*A***) and the phase-rectified signal of a patient who died within the hospital stay (**Fig. 2*B***). In the nonsurviving patient (Fig. 2*B*), oscillations were blunted compared with the surviving patient (Fig. 2*A*).

In line with previous studies, patients were stratified according to DC to following risk categories: DC category 0 = low risk (> 4.5 ms); DC category 1 = intermediate risk (2.5–4.5 ms); and DC category 2 = high risk (≤ 2.5 ms) (23).

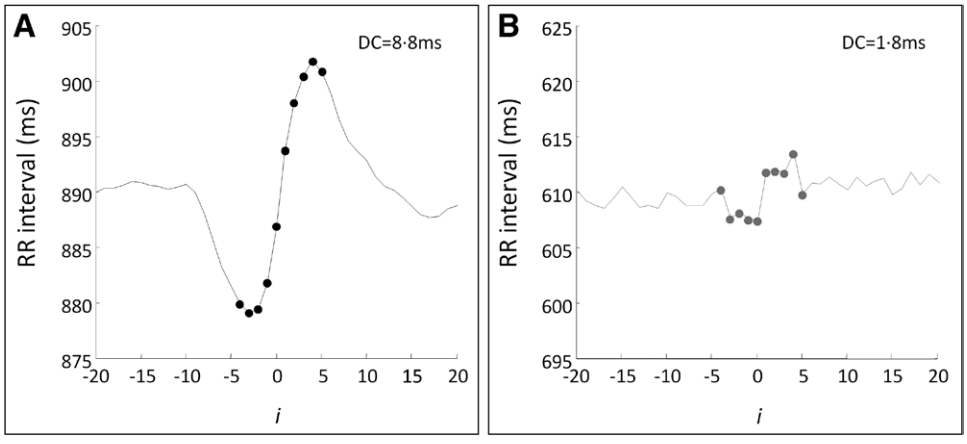

Figure 2. Representative phase-rectified signals from 10-min recordings of heartbeat intervals in one patient who survived the hospital stay (**A**) and one patient who died during the hospital stay (**B**). In the surviving patient, the amplitude of the phase-rectified signal is significantly greater compared with the nonsurviving patient. Bolded points = values of phase-rectified signal used for computation of deceleration capacity (DC), *i* = index of phase-rectified signal *X(i)*.

Assessment of Standard and Complexity Measures of HRV

For assessment of standard and complexity measures of HRV, the first 30 minutes of the recordings were analyzed. In cases of lower recording time, the total length of the recording was used. Measures of HRV were calculated for segments of 256 RR intervals and subsequently averaged. Segments with excessive artifact burden (> 50%) were disregarded. We assessed following standard measures of HRV in the time and frequency domain in line with recommendations of the task force (9): the standard deviation of all normal-to-normal intervals (SDNNs), the HRV index, the root mean square of the successive difference, the power in the low frequency (LF; 0.04–0.15 Hz) and high frequency (HF) ranges (0.15–0.4 Hz), and the ratio between LF and HF. We also assessed two complexity measures of HRV, SampEn and the MSE index. For calculation of SampEn, we used $m = 2$ and $r = 6$ ms in line with previous reports (12). MSE index was defined as the summation of the SampEn values for scales 1–4 (12).

Assessment of the MEWS

The MEWS was calculated from physiological variables, including respiratory rate, heart rate, systolic BP, and body temperature and level of consciousness at ED admission, as previously described (7). The MEWS can range from 0 (lowest risk) to 14 (highest risk).

Study Endpoints

The primary endpoint was intrahospital mortality. Secondary endpoints were total mortality at 30 and 180 days as well transfer to the ICU during the hospital stay.

Follow-Up

Intrahospital deaths were monitored via the electronic hospital information system. Patients were followed up at intervals of 30 and 180 days after admission to the ED. Information about the patient's status after ED discharge was also derived from the hospital information system in patients who were readmitted to the hospital. The status at 30 days after admission to the ED was available in all patients. The status at 180 days after admission to the ED was available in 97.5% of the patients. Patients who were lost to follow-up were censored at the date of latest contact.

Statistical Analyses

Continuous variables are presented as the mean and SD and were compared using the Mann-Whitney *U* test. Qualitative data are expressed

as percentages and were analyzed using the chi-square test. Receiver-operator characteristic (ROC) curves were constructed for all tested predictors by plotting 1 – specificity versus sensitivity. ROC curves were quantified by the area under the curve (AUC). To test the difference between ROC curves, we used bootstrapping based on the creation of pseudo-replicate datasets by random resampling of the dataset *n* times for error estimation ($n = 1{,}000$ in this study) (28). The association of risk variables with the primary endpoint was tested by univariable and multivariable logistic regression analyses. Multivariable analyses were adjusted for age and gender. In logistic regression analyses, coefficients were standardized by the procedure suggested by Menrad (29). To test the incremental prognostic value of DC on top of the MEWS model, we implemented *C*-statistic and integrated discrimination improvement (IDI) score (30). Mortality rates were estimated by the Kaplan-Meier method (31). Odds ratios are presented with 95% CIs. Differences were considered statistically significant when *p* value is less than 0.05. Statistical analyses were performed using CRAN R 2.15.2 and SPSS 20.0 (SPSS: IBM, Armonk, NY).

Sample Size Calculation

The sample size was defined by the number of endpoints with a maximum of 10,000 patients to be screened. Based on previous work, we postulated that 10 endpoints per risk predictor should be on hand (32). We aimed to include a sample size with at least 100 patients reaching the primary endpoint, which allows for multivariable analysis with more than 10 variables to be included.

RESULTS

Table 1 shows the patients' characteristics. Main causes for admission to the ED were cardiovascular and gastrointestinal diseases followed by oncologic, hematologic, and pulmonary diseases. During the hospital stay, 142 patients died (2.5%). After 30 and 180 days, these figures were 196 (3.4%) and 436 patients (7.6%), respectively. As shown in **Table 2**, nonsurviving patients were older and had higher heart rates and respiratory rates but lower systolic, mean, and diastolic arterial blood pressures and low levels of consciousness. Correspondingly, the MEWS score was substantially higher in nonsurviving than surviving patients (3.5 ± 1.7 vs 2.3 ± 1.4; $p < 0.001$).

Table 3 shows the statistical association of markers of HRV with intrahospital mortality. DC was significantly lower in nonsurvivors than survivors (2.9 ± 2.1 ms vs 5.6 ± 2.9 ms; $p < 0.001$). Also standard and complexity measures of HRV were highly significantly associated with the primary endpoint. Nonsurviving patients had lower levels of time and frequency domain measures of HRV ($p < 0.001$ for all) as well as lower levels of SampEn and MSE-index ($p < 0.001$ for both). Table 3 also shows the areas under the ROC curves for prediction of intrahospital mortality. Among all HRV measures tested, DC yielded the greatest area under the curve followed by the HRV index and the MSE index.

TABLE 1. Patients' Characteristics and Outcomes of the Study Population

No. of patients	5,730
Age	61.2 ± 17.7
Female (%)	2,605 (45.5)
Main causes for emergency department admission, *n* (%)	
Cardiovascular	3,427 (59.8)
Gastrointestinal	565 (9.9)
Oncological and hematologic	214 (3.7)
Pulmonary	412 (7.2)
Endocrinologic	128 (2.2)
Infectiologic	178 (3.1)
Renal	49 (0.9)
Other	757 (13.2)
Admission to ICU (%)	366 (6.4)
Duration of hospital stay (d)	6.1 ± 8.9
Intrahospital deaths (%)	142 (2.5)
Deaths at 30 days (%)	196 (3.4)
Deaths at 180 days (%)	436 (7.6)

Table 4 shows the univariable and multivariable logistic regression analyses for prediction of intrahospital mortality. On univariable analysis, the MEWS and all measures of HRV were significantly associated with intrahospital mortality. On multivariable analysis, however, only the MEWS and DC provided independent prognostic information (standardized coefficients of 1.14 and 0.85, respectively; $p < 0.001$ for both). All other markers of HRV were not independently associated with intrahospital mortality.

Figure 3 shows the ROC curve analyses for prediction of intrahospital mortality by DC, the MEWS, and the combination of DC and the MEWS. DC yielded an AUC of 0.780 (95% CI, 0.745–0.813; $p < 0.001$) (**Fig. 3*A***). The MEWS model yielded an AUC of 0.706 (0.667–0.750; $p < 0.001$) (**Fig. 3*B***). Implementing DC into the MEWS model led to a highly significant increase of the AUC to 0.804 (0.770–0.835; $p < 0.001$ for difference) (Fig. 3*B*). The relative IDI was 60% ($p < 0.001$).

Using the established risk categories, DC classified 3,595 (62.7%), 1,157 (20.2%), and 901 (15.7%) patients as low-risk (DC category 0), intermediate-risk (DC category 1), and high-risk patients (DC category 2), respectively. Of these, 26 (0.7%), 39 (3.4%), and 77 patients (7.9%) died during the hospital stay ($p < 0.001$). We also assessed whether DC was a predictor of long-term mortality. **Figure 4** shows cumulative 180-day mortality rates of patients stratified by DC categories. At 30 days, cumulative mortality rates were 0.9%, 5.5%, and 10.1% in the low-, intermediate-, and high-risk groups, respectively ($p < 0.001$). At 180 days, these figures were 2.7%, 12.0%, and 21.0%, respectively ($p < 0.001$).

TABLE 2. Statistical Association of Clinical and Physiological Markers With Intrahospital Mortality

Variable	Survivors	Nonsurvivors	*p*
Demographics			
Patient age (yr)	60.9 ± 17.8	70.5 ± 12.9	< 0.001
Female, %	45.5	43.0	0.386
Physiologic markers			
Heart rate (beats/min)	83.5 ± 24.9	95.6 ± 23.7	< 0.001
Mean blood pressure (mm Hg)	96 ± 18	84 ± 18	< 0.001
Systolic blood pressure (mm Hg)	144 ± 26	125 ± 28	< 0.001
Diastolic blood pressure (mm Hg)	79 ± 19	68 ± 15	< 0.001
Respiratory rate (breaths/min)	16.5 ± 1.8	17.5 ± 1.9	< 0.001
Body temperature (°C)	36.2 ± 0.7	36.2 ± 0.8	0.783
Level of consciousness (according to the alert, voice, pain, unresponsive scale) (%)			
Alert	5,454 (97.6)	135 (95.1)	< 0.001
Reaction to voice	37 (0.6)	6 (4.2)	
Reaction to pain	96 (1.7)	1 (0.7)	
Unresponsive	1 (< 0.1)	0 (0)	
Modified early warning score (score points)	2.3 ± 1.4	3.5 ± 1.7	< 0.001

Cause of admission had no significant influence on the predictive value of DC. DC was a significant predictor of mortality in the 3,427 patients admitted for cardiovascular causes (AUC, 0.767 [0.707–0.827]; $p < 0.001$) as well as in the 2,303 patients admitted for noncardiovascular causes (AUC, 0.768 [0.725–0.811]; $p < 0.001$). Furthermore, DC was significantly lower in the 366 patients who were transferred to the ICU during their hospital stay than in patients who were not transferred (3.8 ± 2.7 ms vs 5.7 ± 2.9 ms; $p < 0.001$).

DISCUSSION

The main findings of our study indicate that DC is a strong predictor of intrahospital mortality in patients admitted to a medical ED. Its prognostic value was independent of established measures of HRV and significantly improved the MEWS model, which is an established scoring system for early risk stratification in the ED. The predictive power of DC was comparable for patients admitted for cardiovascular and noncardiovascular diseases. DC was also a strong predictor of 30-day and 180-day mortality.

Previous studies have shown that reduced HRV is associated with poor outcome in various cardiac and noncardiac diseases (14–16, 18–21). However, only very few studies tested the clinical usefulness of HRV as clinical tool for risk prediction in a medical ED (33). DC differs from standard measures of HRV in several aspects. First, due to its underlying signal processing algorithm, DC is robust to artifacts, noise, and nonstationarities. This is of particular advantage when analyzing biological signals that are recorded under uncontrolled conditions in the setting of an ED (25). Second, DC is an integral measure of all deceleration-related periodic components of HRV, irrespective of their frequency. Thus, DC is not driven by any specific physiological mechanism but rather influenced by alterations of the vagal, sympathetic, vascular, and humoral systems. Thereby, DC differs from traditional spectral measures of HRV, which assess the spectral power in distinct frequency bands. Global measures of HRV, such as SDNN or HRV index, also include nonperiodic patterns of HRV, which might not be directly related to autonomic mechanisms.

In contrast to previous studies (23), DC was assessed from short-term ECG recordings, which raises both methodological and physiological questions. First, the number of segments entering the PRSA-averaging process is much smaller compared to a full 24-hour Holter recording that might limit the capability of eliminating noise and artifacts. Second, short-term DC does not reflect ultra and very low-frequency oscillations. DC as assessed in the present study should therefore be interpreted as measure of short-term cardiovascular control.

In our study, the prognostic performance of DC was statistically superior to that of other measures of HRV. However, it needs to be emphasized that direct comparisons between DC and other metrics might be difficult. Several requirements for assessment of traditional measures of HRV, particularly in the frequency domain, were not met, including stationarity of the signal and manual preprocessing of the raw data (9). Notably, the complexity measures SampEN and MSE index that quantify the amount predictability of the signal were strong predictors of mortality in our population. As previous studies have

TABLE 3. Statistical Association of Markers of Heart Rate Variability With Intrahospital Mortality

Variable	Survivors	Nonsurvivors	*p*	Area Under the Receiver-Operator Characteristic Curve (95% CI)	*p*
Deceleration capacity	5.6 ± 2.9	2.9 ± 2.1	< 0.001	0.780 (0.745–0.813)	< 0.001
Standard deviation of all normal to-normal intervals	42.7 ± 29.6	29.3 ± 21.4	< 0.001	0.658 (0.608–0.708)	< 0.001
Root mean square of successive differences of all normal-to-normal intervals	22.6 ± 12.6	19.8 ± 12.3	< 0.001	0.598 (0.542–0.654)	< 0.001
Heart rate variability triangular index	6.0 ± 2.9	3.8 ± 2.3	< 0.001	0.744 (0.699–0.789)	< 0.001
LF	614.1 ± 1229.3	348.8 ± 783.3	< 0.001	0.662 (0.611–0.712)	< 0.001
HF	187.0 ± 270.5	128.0 ± 182.0	< 0.001	0.602 (0.548–0.656)	< 0.001
LF/HF	3.8 ± 4.2	2.5 ± 3.2	< 0.001	0.654 (0.606–0.701)	< 0.001
Sample entropy	1.8 ± 0.5	1.4 ± 0.5	< 0.001	0.677 (0.625–0.729)	< 0.001
Multiscale entropy index	5.0 ± 2.1	3.2 ± 2.0	< 0.001	0.736 (0.689–0.783)	< 0.001

LF = power in the low-frequency range, HF = power in the high-frequency range.

shown that SampEN and MSE index are highly sensitive to their respective input variables *m*, *r*, and scale (12), future studies are needed to test whether the prognostic ability of these complexity measures might be optimized by refined settings.

We assessed the predictive value of DC and the MEWS model by ROC curve analysis, which is independent from selection of specific cutoff values. The largest separation of ROC curves between DC and the MEWS model occurred at high sensitivity levels of 80%. At this level of sensitivity, the corresponding specificity of DC was substantially higher than that of the MEWS model. Hence, DC-based risk assessment is particularly useful for a better identification

TABLE 4. Univariable and Multivariable Binary Logistic Regression Analysis for Prediction of Intrahospital Mortality

	Univariable Analysis			Multivariable Analysis		
Variable	OR (95% CI)	*z*	*p*	OR (95% CI)	*z*	*p*
Modified early warning score	1.28 (1.22–1.35)	9.7	< 0.001	1.14 (1.09–1.19)	5.8	< 0.001
deceleration capacity	0.75 (0.71–0.79)	10.0	< 0.001	0.81 (0.74–0.89)	4.3	< 0.001
Standard deviation of all normal to-normal intervals	0.83 (0.79–0.89)	5.5	< 0.001	1.01 (0.92–1.11)	0.2	0.835
Root mean square of successive differences of all normal-to-normal intervals	0.93 (0.87–0.98)	2.5	0.012	1.05 (0.97–1.13)	1.2	0.213
Heart rate variability triangular index	0.76 (0.72–0.81)	8.3	< 0.001	0.91 (0.75–1.11)	0.9	0.358
LF	0.90 (0.84–0.97)	2.9	0.003	1.01 (0.92–1.10)	0.2	0.879
HF	0.92 (0.86.0.98)	2.5	0.011	0.98 (0.90–1.07)	0.4	0.687
LF/HF	0.88 (0.82–0.94)	3.9	< 0.001	0.99 (0.93–1.07)	0.1	0.886
Sample entropy	0.83 (0.78–0.88)	6.3	< 0.001	0.99 (0.89–1.09)	0.3	0.778
Multiscale entropy index	0.77 (0.72–0.82)	8.6	< 0.001	1.01 (0.83–1.23)	0.1	0.913

OR = odds ratio, LF = power in the low-frequency range, HF = power in the high-frequency range.
Multivariable analysis adjusted for age and gender; standardized coefficients presented.

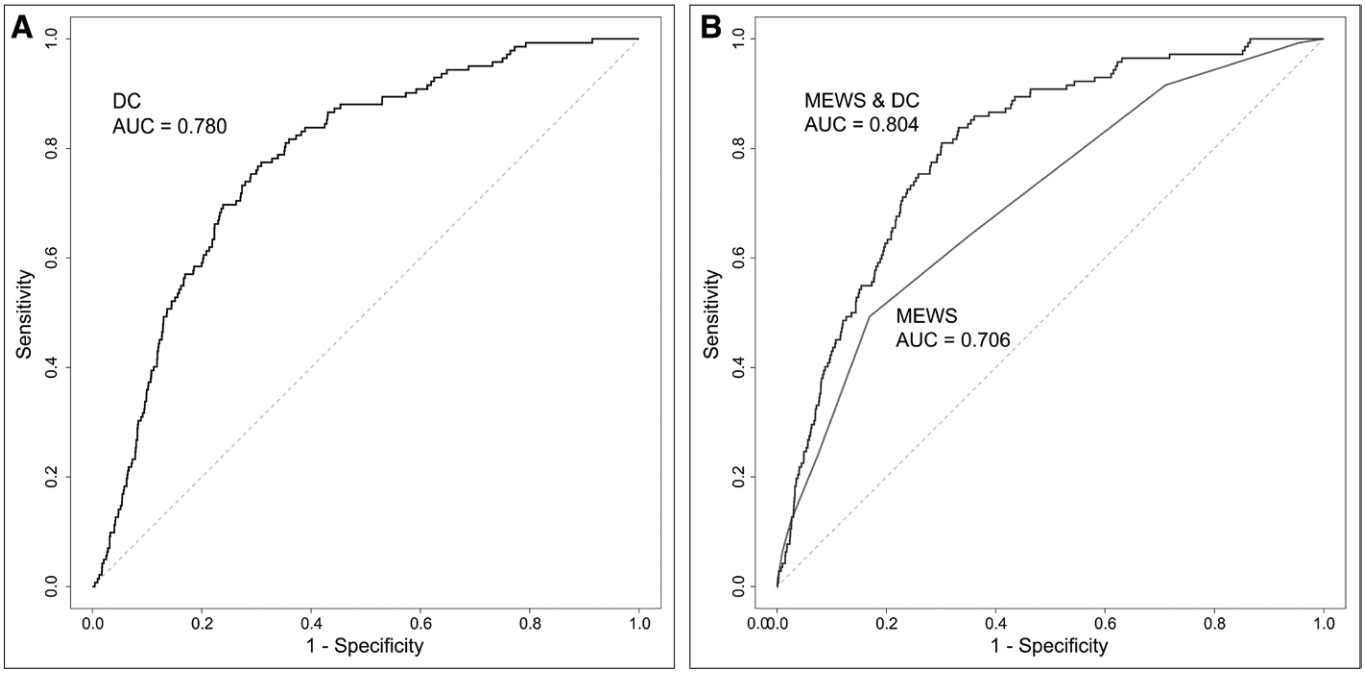

Figure 3. Receiver-operator characteristic curves for prediction of intrahospital mortality. **A**, Deceleration capacity (DC). **B**, The modified early warning score (MEWS) as well as the combination of the MEWS and DC. The difference between the area under the receiver-operator characteristic curve (AUC) of the MEWS and the combination of the MEWS and DC was highly significant ($p < 0.001$).

of low-risk patients who could be treated with less priority. This was also confirmed when using DC risk categories. DC greater than 4.5 ms classified almost two thirds of patients as low-risk patients. These patients were at very low risk of death (0.7%; 26 deaths in 3,595 patients). By contrast, DC less than or equal to 2.5 ms identified a smaller high-risk group of 978 patients (17% of admitted patients) who were at an almost 12-fold risk of death compared with the low-risk group. Our findings therefore suggest that these patients should be treated with high priority. In this context of note, impaired DC at admission also predicted later transfer to the ICU. Extended follow-up to 6 months revealed that impaired DC was also a strong predictor of late mortality. Patients with DC less than or equal to 2.5 ms at admission had a cumulative 6-month mortality rate of 21%, indicating that these patients should be closely monitored after discharge. Importantly, risk predictive power of DC was equally strong in both cardiovascular and noncardiovascular patients. It needs to be mentioned that the used cutoff values have been derived from 24-hour Holter recordings in postinfarction patients. Post hoc analyses revealed an optimum cutoff value of 3.2 ms for DC in the study population, which needs to be validated in further studies.

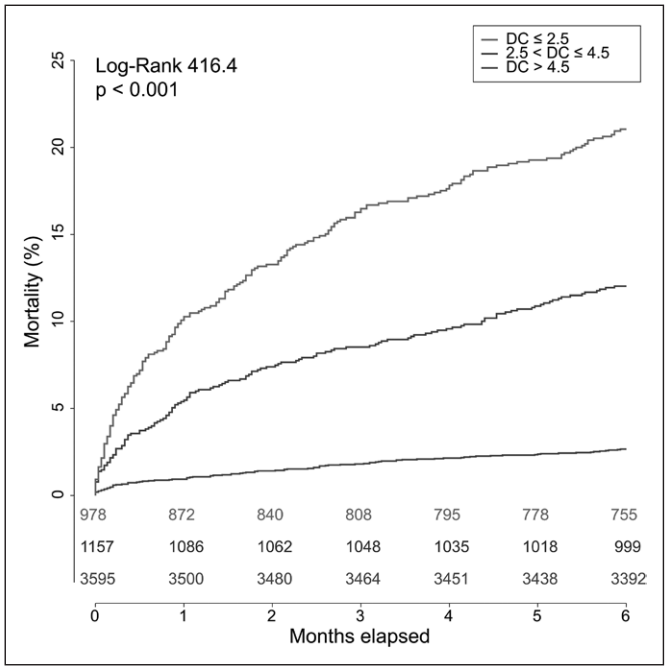

Figure 4. Cumulative 180-day mortality rates in patients stratified by deceleration capacity (DC) risk categories. The numbers of patients in the individual groups involved in the analysis at 0, 45, 90, 135, and 180 days are shown under the graph.

The limitations of our study need to be recognized. First, autonomic function by means of HRV can only be assessed in patients with sinus rhythm. Second, our study was performed in a medical ED. Further investigations are necessary to determine whether DC provides prognostic value in different settings. Furthermore, we did not compare the predictive value of DC to biochemical markers such as the sensitive troponins or C-reactive protein. We also cannot rule out that assessment of other markers might have influenced triage in our ED. Finally, as our study was purely observational, it needs to be shown whether clinical decision making based on DC and other predictors leads to a better outcome.

CONCLUSIONS

In conclusion, assessment of the ANS activity by DC provides strong and independent prognostic information in patients admitted to a medical ED. DC can be obtained fully automatically within minutes at first contact and significantly improves established risk stratification models. The technology is inexpensive, readily available, and can be implemented in existing monitoring devices. Further technical developments might realize the integration of the technology into cheaper mobile devices, which could be used in waiting halls of ED or in ambulatory settings.

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