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Early Risk Stratification of Patients After Successfully Resuscitated Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation—The Angiography After Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation (TOMAHAWK) Risk Score

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OBJECTIVES: Existing scores for risk stratification after out-of-hospital cardiac arrest (OHCA) are either medically outdated, limited to registry data, small cohorts, and certain healthcare systems only, or include rather complex calculations. The objective of this study was to develop an easy-to-use risk prediction score for short-term mortality in patients with successfully resuscitated OHCA without ST-segment elevation on the post-resuscitation electrocardiogram, derived from the Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation (TOMAHAWK) trial. The risk score was externally validated in the Coronary Angiography after Cardiac Arrest Trial (COACT) cohort (shockable arrest rhythms only) and additional hospitals from Berlin, Germany (shockable and nonshockable arrest rhythms).

DESIGN: Predefined subanalysis of the TOMAHAWK trial.

SETTING: Development and external validation across 52 centers in three countries.

PATIENTS: Adult patients with successfully resuscitated OHCA and no ST-segment elevations.

INTERVENTIONS: Utilization of the TOMAHAWK risk score upon hospital admission.

MEASUREMENTS AND MAIN RESULTS: The risk score was developed using a backward stepwise regression analysis. Between one and four points were attributed to each variable in the risk score, resulting in a score with three risk categories for 30-day mortality: low (0–2), intermediate (3–6), and high (7–10). Five variables emerged as independent predictors for 30-day mortality and were used as risk score parameters: age of 72 years old or older, known diabetes, unshockable initial electrocardiogram rhythm, time until return of spontaneous circulation greater than or equal to 23 minutes, and admission arterial lactate level greater than or equal to 8 mmol/L. The 30-day mortality rates for each risk category were 23.6%, 68.8%, and 86.2%, respectively ($p < 0.001$) with a good discrimination at an area under the curve of 0.82. External validation in the COACT and Berlin cohorts showed short-term mortality rates of 23.1% and 20.4% (score 0–2), 44.8% and 48.1% (score 3–6), and 78.9% and 73.3% (score 7–10), respectively (each $p < 0.001$).

CONCLUSIONS: The TOMAHAWK risk score can be easily calculated in daily clinical practice and strongly correlated with mortality in patients with successfully resuscitated OHCA without ST-segment elevation on post-resuscitation electrocardiogram.

KEYWORDS: cardiac arrest; coronary angiography; risk score

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KEY POINTS

Question: Can the Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation (TOMAHAWK) risk score reliably predict 30-day mortality in patients with out-of-hospital cardiac arrest (OHCA) without ST-segment elevation?

Findings: The TOMAHAWK risk score demonstrated robust predictive accuracy in identifying mortality risk showing good calibration and discrimination across internal and external validation cohorts.

Meaning: These results support the TOMAHAWK risk score as a valuable tool for early risk stratification in non-ST-elevation OHCA patients, potentially enhancing clinical decision-making and tailored post-resuscitation care in routine clinical settings.

The prognosis in patients who experienced out-of-hospital cardiac arrest (OHCA) is poor, with a mortality of up to 65% even among those who undergo successful resuscitation and hospital admission (1). Acute coronary syndromes account for up to 60% of OHCA in which a cardiac cause has been identified (2). The finding of ST-segment elevation on the post-resuscitation electrocardiogram has a high predictive value for underlying coronary lesions triggering the cardiac arrest event (3, 4). In the far larger subgroup of OHCA patients without ST-segment elevation, the spectrum of underlying conditions is considerably broader and includes both cardiac and noncardiac causes.

While neurologic prognostication in patients who remain unconscious after OHCA is not recommended until 72 hours after the index event (5–7), accurate risk stratification in the very early period is still important to inform further treatment decisions. Therefore, there remains an obvious need for a risk stratification tool that is simple, easily applicable, and readily available directly after hospital admission.

A number of OHCA risk scores with various combinations of predictors have been developed. However, most of these share certain limitations as they were derived from (retrospective) registry data or few centers, contain complex calculations, were developed/validated multiple years ago or in small cohorts. Indeed, a very recently published scientific statement by the American Heart Association (AHA) highlighted the lack of OHCA risk scores based on prospective data (8).

The aim of this study was to develop a simple, easy-to-use, readily available, fully validated risk score for short-term mortality prediction upon hospital admission in patients after successfully resuscitated OHCA without ST-segment elevation on the post-resuscitation electrocardiogram enrolled in a large randomized controlled trial (RCT) across 31 hospitals from two countries.

The secondary objective was to conduct an external validation of the risk score in distinct cohorts of OHCA patients without ST-segment elevation. This validation encompassed another large RCT across 19 hospitals in the Netherlands, limited to patients with shockable arrest rhythms, alongside three additional hospitals in Berlin, Germany, which included both shockable and nonshockable arrest rhythms.

MATERIALS AND METHODS

The present analysis is a prespecified substudy of the randomized Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation (TOMAHAWK) trial. In this trial, immediate coronary angiography showed no benefit compared with delayed or no coronary angiography in patients after successfully resuscitated OHCA of possible coronary origin without ST-segment elevation on the post-resuscitation electrocardiogram (9–11). Exclusion criteria were patient age younger than 30 years, ST-segment elevation or left bundle branch block (LBBB) on the post-resuscitation electrocardiogram, no return of spontaneous circulation (ROSC) upon hospital admission, severe hemodynamic or electrical instability requiring immediate coronary angiography, obvious extracardiac etiology of OHCA, and in-hospital cardiac arrest and known or likely pregnancy. Patients younger than 30 years were excluded due to the low prevalence of coronary artery disease as an etiology for cardiac arrest in this age group. LBBB was excluded as it is regarded as an electrocardiogram equivalent to ST-segment elevation myocardial infarction, a condition for which the evidence of coronary angiography after cardiac arrest had already been established in the guidelines and was outside the scope of the TOMAHAWK trial. Patients deemed "likely pregnant" were excluded based on clinical suspicion or rapid screening tests. The primary endpoint was 30-day all-cause mortality. The study, which was conducted according to the Declaration of Helsinki, was approved by the local ethics committee (approval date January 2016; title: "Immediate unselected coronary angiography versus delayed triage in survivors of out-of-hospital cardiac arrest without ST-segment elevation"; approval number: "Az: 15-123"; board name: "Ethik-Kommission der Universität zu Lübeck") and all patients or their legal representatives gave written informed consent.

This study was performed according to the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) checklist (**Supplemental Material**, http://links.lww.com/CCX/B472) (12). The model was developed in the "per protocol" population of the TOMAHAWK trial using a multivariable logistic regression analysis with stepwise backward elimination. Unselected multivariable testing was performed including all database variables potentially associated with mortality. Variables significantly related to mortality in multivariable testing ($p < 0.05$) were kept in the model. Herein, five variables remained significantly associated with mortality. These variables constitute the risk score parameters. Only patients with complete datasets for these five risk score variables and 30-day mortality were considered for further testing.

Continuous variables were dichotomized. The cutoff points were defined using Youden's index (13). The scoring system was determined by rounding the respective parameter estimates, attributing values between one and four points to each variable, based on the observed odds ratio (OR). Parameters with a rounded OR of two were assigned one point, those with a rounded OR of three were assigned two points, those with a rounded OR of four were assigned three points, and those with a rounded OR of five were assigned four points. According to the risk score, the population was classified into three risk categories based on the number of patients: low (0–2), intermediate (3–6), and high (7–10). Comparison of 30-day mortality rates was performed by chi-square testing and by Kaplan-Meier analysis with pairwise log-rank testing. Receiver operating characteristic (ROC) analysis was performed to assess discriminative power.

External validation was performed in patients with OHCA, who met the TOMAHAWK inclusion criteria, in the Coronary Angiography after Cardiac Arrest Trial (COACT) cohort (14), another large RCT performed across 19 medical centers in the Netherlands. Given that the COACT trial exclusively included patients with shockable arrest rhythms, external validation was additionally conducted at three independent tertiary care centers in Berlin, Germany, where both shockable and nonshockable arrest rhythms were represented. The Berlin data, which mirrored routine clinical practice, was also used to assess the TOMAHAWK risk score's external applicability beyond the controlled conditions of an RCT. Comparison of 30-day mortality rates in the external validation cohort, according to the different risk score categories, was done by chi-square testing as well as by Kaplan-Meier analyses with pairwise log-rank testing. Furthermore, ROC analyses were performed to assess the discriminative power of the risk score. Calibration of the TOMAHAWK risk score was assessed in the external validation cohort by dividing the sample into five equal groups based on the predicted probability, then plotting the mean probability of each quintile against the observed frequency of 30-day mortality for that group.

All statistical analyses were performed using R Core Team (2022) (R Foundation for Statistical Computing, Vienna, Austria) at the Department of Cardiology, Angiology, and Intensive Care Medicine, Deutsches Herzzentrum der Charité, Berlin, Germany, as being previously published (15).

RESULTS

Of the 495 patients analyzed in the "per protocol"-cohort of the TOMAHAWK trial, 353 patients with complete datasets for the selected variables of the risk score were included in the final cohort (**Fig. 1**). A total of 245 patients (69.4%) were male and the median age was 69 years (interquartile range [IQR], 60–78 yr) (**Table 1**). In 318 patients (90.1%), OHCA was witnessed and cardiopulmonary resuscitation (CPR) was performed by bystanders in 241 patients (68.3%), respectively. ROSC was achieved within 21 minutes (IQR, 14–31 min) on average. Overall mortality within 30 days was 53.5% (189/353 patients died). The most frequent causes of death were neurologic injury or

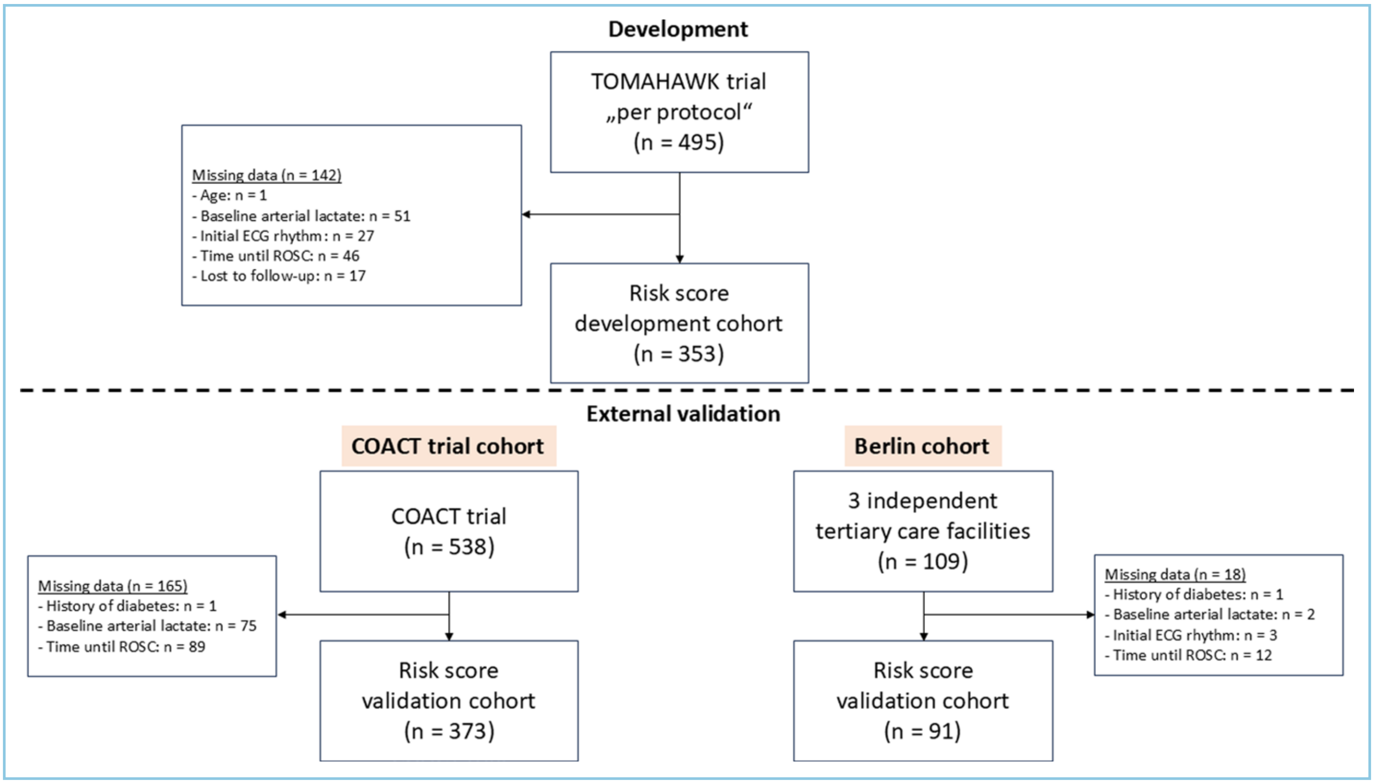

Figure 1. Flow chart of the development and external validation cohort. The development cohort was comprised of patients from the Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation (TOMAHAWK) trial, whereas the external validation cohort was retrieved from Coronary Angiography after Cardiac Arrest Trial (COACT), another large randomized controlled trial in the field, as well as three independent hospitals in Berlin, Germany. In the development and validation cohort, patients with missing data with respect to the risk score variables were excluded. ECG = electrocardiogram, ROSC = return of spontaneous circulation.

anoxic brain damage, circulatory failure, or septic shock (**Supplemental Table 1**, http://links.lww.com/CCX/B473).

The aforementioned final cohort used for the TOMAHAWK risk score development was compared with patient characteristics and mortality outcomes of patients who were excluded from the risk score development. Ruling out severe exclusion bias, both cohorts were similar across all variables, except for a statistical but not numerically relevant difference in time until ROSC (**Supplemental Table 2**, http://links.lww.com/CCX/B473).

Variable Identification and Risk Score Development

After multivariable testing, the following five variables remained statistically significant predictors and were included in the model: age of 72 years old or older, history of diabetes, unshockable initial electrocardiogram rhythm, time until ROSC greater than or equal to 23 minutes, and admission arterial lactate levels greater than or equal to 8 mmol/L. The results of the regression analysis are shown in **Table 2**. Subsequently, the TOMAHAWK risk score was created attributing between zero and four points to the variables based on the OR (**Fig. 2**) leading to a risk score with a minimum of 0 and a maximum of ten points. Using the risk score, the population was classified into three risk categories: low (0–2), intermediate (3–6), and high (7–10), as shown in Figure 2. Of 353 patients, 144 patients (40.8%) were classified to be at low risk, 144 patients (40.8%) at intermediate risk, and 65 patients (18.4%) at high risk.

The analysis was repeated by entering lactate values and time until ROSC as continuous variables. In this sensitivity analysis, there were no relevant differences compared with the analysis with dichotomized variables. The five selected parameters remained significant after multivariable testing as in the primary analysis. Notably, the attribution of one to four points according to the rounded ORs for determination of the scoring system

TABLE 1.
Baseline Characteristics

Characteristics	Development: Angiography After Out-of-Hospital Cardiac Arrest Without ST-Segment Elevation Cohort (TOMAHAWK) ($n = 353$)	External Validation: Coronary Angiography After Cardiac Arrest Trial (COACT) Cohort ($n = 373$)	External Validation: Berlin Cohort ($n = 91$)
Demographic data			
Age (yr)	69 (60–78)	67 (59–75)	68 (57–77)
Male sex	245 (69.4%)	293 (78.6%)	66 (72.5%)
Body mass index (kg/m²)	27 (25–29)	NA	26 (25–31)
Cardiovascular risk factors or cardiovascular diseases			
Arterial hypertension	217 (61.5%)	177 (47.5%)	57 (62.6%)
Diabetes mellitus	96 (27.2%)	71 (19.0%)	19 (20.9%)
Heart failure	59 (16.7%)	NA	23 (25.3%)
History of stroke	27 (7.6%)	22 (5.9%)	7 (7.7%)
Cardiac arrest data			
Witnessed cardiac arrest	318 (90.1%)	312 (83.6%)	74 (81.3%)
Bystander cardiopulmonary resuscitation	241 (68.3%)	291 (78.0%)	74 (81.3%)
Unshockable initial electrocardiogram rhythm	167 (47.3%)	0 (0%)	27 (29.7%)
Time until return of spontaneous circulation (min)	21 (14–31)	15 (8–20)	19 (12–27)
Hospital treatment			
Vasopressor use on hospital admission	249 (70.5%)	110 (70.5%)	36 (39.6%)
Coronary angiography			
None	78 (22.1%)	74 (19.8%)	18 (19.8%)
Within 24 hr	191 (54.1%)	206 (55.2%)	59 (64.8%)
After 24 hr	75 (21.2%)	93 (24.9%)	14 (15.4%)
Targeted temperature management	277 (78.5%)	351 (94.1%)	67 (73.6%)
Laboratory results			
Baseline arterial creatinine (mg/dL)	1.28 (1.05–1.63)	1.15 (0.98–1.31)	1.29 (1.09–1.52)
Baseline arterial lactate (mmol/L)	4.7 (2.5–8.3)	5.01 (2.9–8.6)	1.29 (1.09–1.52)
Outcome			
30-d mortality	189 (53.5%)	124 (33.2%)	34 (37.4%)

NA = not available.
Values are displayed as median (interquartile range) or frequency (percent).

also remained unchanged (**Supplemental Table 3**, http://links.lww.com/CCX/B473).

Per the score risk categories of low, intermediate, and high, the observed mortality rates assessed by chi-square testing were 34 (23.6%), 99 (68.8%), and 56 (86.2%), respectively ($p < 0.001$). Figure 2 depicts the Kaplan-Meier curves for 30-day mortality according to the three risk score categories. In C-statistics, the predictive value of the risk score with respect to 30-day mortality was good with an area under the curve (AUC) of 0.82 (95% CI, 0.77–0.86).

TABLE 2.
Results of Multivariable Logistic Regression Analysis

Predictors	OR (95% CI)	Parameter Estimate	p
Age ≥ 72 yr	3.36 (2.03–5.63)	1.21	< 0.001
Diabetes mellitus	1.88 (1.06–3.37)	0.63	0.031
Unshockable initial electrocardiogram rhythm	2.58 (1.56–4.31)	0.95	< 0.001
Return of spontaneous circulation ≥ 23 min	2.42 (1.46–4.03)	0.88	0.001
Baseline arterial lactate ≥ 8 mmol/L	5.09 (2.75–9.83)	1.63	< 0.001

OR = odds ratio.

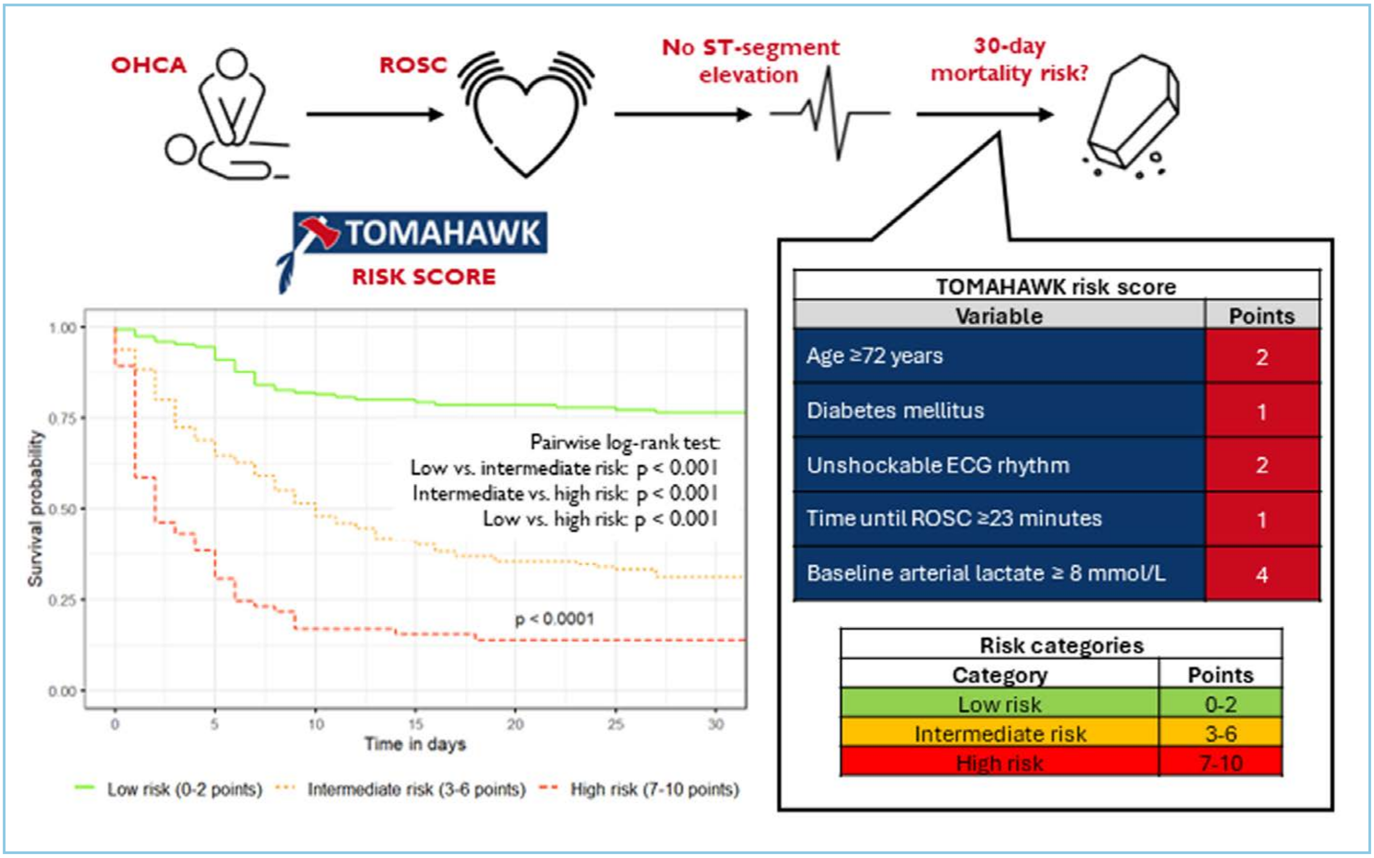

Figure 2. Successfully resuscitated out-of-hospital cardiac arrest (OHCA) without ST-segment elevation—the Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation (TOMAHAWK) risk score. Using a stepwise multivariable regression analysis, a risk score for mortality was developed in patients with successfully resuscitated OHCA without ST-segment elevation on the post-resuscitation electrocardiogram (ECG). The risk score was determined by rounding the respective odds ratios, attributing 1–4 points to each variable and the total score separated by risk category: low (0–2 points), intermediate (3–6 points), and high (7–10 points). In total, 353 patients in the development cohort were classified according to the TOMAHAWK risk score into the low-risk (n = 144, 40.8%), intermediate-risk (n = 144, 40.8%), or high-risk (n = 65, 18.4%) categories. The Kaplan-Meier analysis for 30-d mortality showed a significant, stepwise increase in mortality with a good predictive value with an area under the curve of 0.82 (95% CI, 0.77–0.86). ROSC = return of spontaneous circulation.

External Validation of Risk Score

For external validation, patients with OHCA who fulfilled the TOMAHAWK trial inclusion criteria were included: 373 patients from the COACT cohort and 91 patients from three independent tertiary care centers in Berlin, Germany (Fig. 1 and Table 1). Among these, 229 (61.4%) were categorized as low risk, 125

(33.5%) as intermediate risk, and 19 (5.1%) as high risk in the COACT cohort, compared with 49 (53.8%), 27 (29.7%), and 15 (16.5%) in the Berlin cohort, respectively. Within each cohort, 124 (33.2%) and 34 (37.4%) patients, respectively, died within 30 days.

The external validation yielded consistent findings: Mortality rates across risk categories in chi-square tests were 53 (23.1%), 56 (44.8%), and 15 (78.9%) in the COACT cohort, as well as 10 (20.4%), 13 (48.1%), and 11 (73.3%) in the Berlin cohort (each with $p < 0.001$). **Figure 3** presents Kaplan-Meier survival curves with pairwise comparisons by log-rank tests (low vs. intermediate risk: $p < 0.001$ for COACT, $p = 0.018$ for Berlin; intermediate vs. high risk: $p < 0.001$ for COACT, $p = 0.014$ for Berlin; low vs. high risk: $p < 0.001$ in both cohorts). Comparison of predicted probabilities against observed 30-day mortality frequencies by risk score quintiles showed robust calibration in both the COACT and Berlin cohorts (**Supplemental Fig. 1**, http://links.lww.com/CCX/B473). C-statistics indicated good discriminative performance: the COACT cohort achieved an AUC of 0.73 (95% CI, 0.68–0.79), while the Berlin cohort had an AUC of 0.77 (95% CI, 0.66–0.87) (**Supplemental Fig. 2**, http://links.lww.com/CCX/B473).

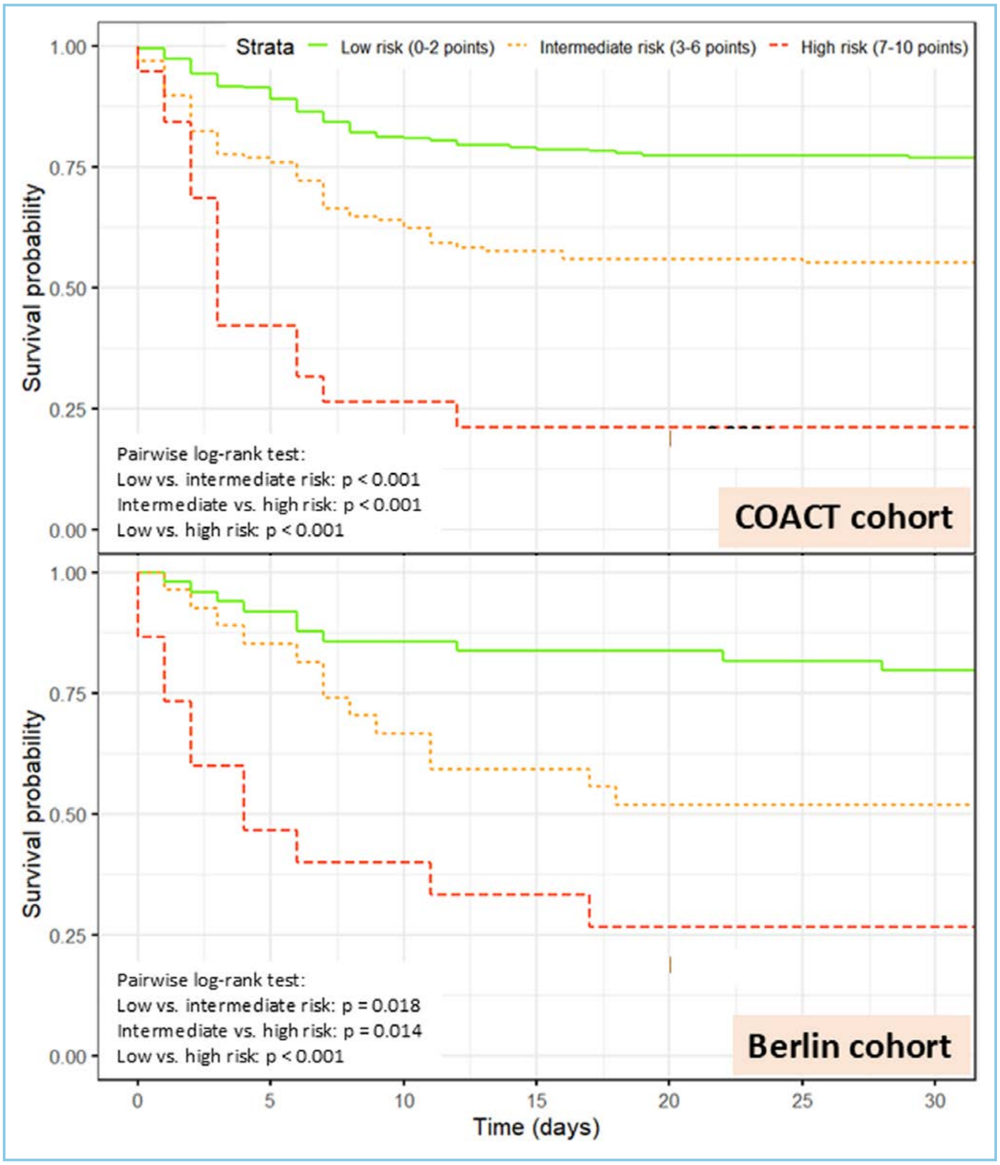

Figure 3. Angiography after Out-of-Hospital Cardiac Arrest without ST-Segment Elevation (TOMAHAWK) risk score external validation analysis in the Coronary Angiography after Cardiac Arrest Trial (COACT) and Berlin cohorts. For validation, Kaplan-Meier analyses for 30-d mortality according to the TOMAHAWK risk score categories were performed for the external validation cohorts retrieved from COACT and three independent hospitals in Berlin, Germany. Kaplan-Meier curves estimate survival over time, with the *X*-axis showing time (30 days) and the *Y*-axis displaying survival probability. The analyses show a significant increase in mortality rates per the risk score categories: the low-risk group had the highest survival, followed by the intermediate-risk group, while the high-risk group had the lowest survival. These findings validate the TOMAHAWK risk score's ability to predict outcomes effectively.

DISCUSSION

The TOMAHAWK risk score was developed for prognostication of short-term mortality in patients with successfully resuscitated OHCA without ST-segment elevation. There are four major strengths of the TOMAHAWK risk score. First, the risk score was developed in a homogenous population of patients with resuscitated OHCA without ST-segment elevation in a large RCT and validated in another large RCT as well as in routine clinical data from additional hospitals, ensuring applicability beyond the controlled conditions of an RCT. All in all, 52 centers in three countries contributed to risk score development and validation. Second, the risk score includes simple variables from clinical practice that are readily available on hospital admission and can be rapidly calculated. Third, the risk score showed good discriminatory power regarding mortality by accurately discriminating three risk groups. Fourth, the external validation of the risk score showed strong correlations with mortality and a good risk score calibration.

Need for Early Clinical Prognostication After Out-of-Hospital Cardiac Arrest

Given unacceptably high mortality rates, early prognostication in patients with OHCA seems to be crucial but still remains challenging, particularly in patients with prolonged coma after successful resuscitation. Multiple predictors are used during post-resuscitation care, such as neurologic examination in adjunct to brain imaging, electroencephalogram, evoked potentials, and blood biomarkers (7). However, most of the aforementioned diagnostic measures can only be performed or interpreted after several days following the index event, resulting in significant delays (5). In contrast, the TOMAWHAWK risk score allows for early risk stratification at time of hospital admission and could support clinicians with better definitions of therapy goals and adequate resource allocation. Particularly, in patients with poor outcome predictions, unfavorable clinical courses can be anticipated and treatment adjusted accordingly. Given the simplicity of the TOMAHAWK risk score (sum of points without nomograms, transformations, or complex calculations), it could be easily applied as part of routine clinical practice and facilitate standardization of post-resuscitation care across medical centers. Notably, utilization of a single risk score should not solely guide therapy decisions but would certainly provide valuable support for clinicians to guide their decisions. The TOMAHAWK score is intended for early risk stratification and complements, rather than replaces, formal neuroprognostication protocols. Its use could provide valuable initial insights while adhering to established guidelines for delayed and protocolized neuroprognostication. Beyond mortality prediction, the TOMAHAWK score could potentially guide therapeutic prioritization, resource allocation, and family discussions about goals of care. By providing early, actionable insights, the score may enhance decision-making during the critical post-resuscitation phase, including identifying patients who might benefit from advanced therapies or palliative approaches.

Risk Scores for Patients With Out-of-Hospital Cardiac Arrest

Different risk prediction instruments for OHCA patients have been developed but show limitations, such as the "Acute Physiology and Chronic Health Evaluation (APACHE) II score," the "OHCA score," the "Cardiac Arrest Hospital Prognosis (CAHP) score," the "missed arrest, initial rhythm, reactivity of pupils, chanigng rhythm, low pH and epinehrine ($MIRACLE_2$) score," and the "Target Temperature Management (TTM) trial score" (16–19). The AHA emphasized a lack of prospective data for OHCA risk scores in a very recently published scientific statement (8). First, although the "APACHE II" score is widely used to predict mortality of general ICU patients, it is not tailored to the specific features of OHCA patients. Compared with the TOMAHAWK risk score, insufficient prognostic performance with an AUC of 0.62 at admission was reported for OHCA patients with the "APACHE II" score (20). Second, the "OHCA score," the "CAHP score," and the "$MIRACLE_2$ score" were developed in (retrospective) registry data only, exposing the risk scores to substantial limitations. Particularly, the "OHCA score" was developed in a relatively small cohort of 130 patients treated at one medical center. Conversely, the TOMAHAWK risk score was derived from two large RCTs and routine clinical data following strict rules on standardized medical treatment (including therapy withdrawal) and data collection. Although the "TTM score" was also derived from a RCT (21), important variables with missing values were imputed, which reduces precision, and no external validation was performed. Imputation was not performed to develop the TOMAHAWK score. Third, the "OHCA score" and the "CAHP score" were developed and validated only in French medical centers, while the "$MIRACLE_2$ score" was developed in medical centers in London, United Kingdom, limiting their clinical use to specific healthcare systems. Indeed, external validation of the "$MIRACLE_2$ score" in Slovenia showed a significant loss in predictive performance (18). The TOMAHAWK risk score was developed across 31 medical centers in Germany and Denmark, and externally validated across 19 centers in the Netherlands and three centers in Germany. Fourth, the "TTM score" was derived from patients, which were treated with therapeutic hypothermia. In contrast, the "OHCA score" was developed in patients treated before the year 2003, with therapeutic hypothermia being performed in 14% of the development cohort compared with 74% of the validation cohort, indicating not only strong study heterogeneity but also changing medical practice during the study period. Current guidelines recommend active fever prevention and highlight the current state of insufficient evidence for or against active cooling in light of the recent TTM2 trial (22, 23). A recent meta-analysis showed no mortality difference between hypothermia and normothermia (24). Apart from progressing evidence on temperature control in OHCA patients, multiple other major improvements have occurred since the development of the "OHCA score" in 2006, such as improved emergency medical infrastructures ("Systems saving lives," including mobile phone-assisted CPR, smartphone-based alert systems for nearby laypersons, digital mapping of automated external defibrillators [AEDs] locations, and increased AED availability) (25), as well as increased use of mechanical CPR devices (26) and epinephrine by paramedics (27) or improved airway management strategies during OHCA (28). Hence, multiple OHCA risk scores may not reflect current guideline-based clinical practice and improvements in cardiac arrest therapy, while the TOMAHAWK risk score used data from recent medical practice. Fifth, the "OHCA score" and the "CAHP score" are rather difficult to use, particularly in a strenuous setting like cardiac arrest treatment. The "OHCA score" is a complex equation, including natural logarithms, decimal fractions as well as additions and subtractions. For the "CAHP score," clinicians are supposed to use a nomogram to locate the patient values on different axes, draw a line to the point axis, and calculate the sum, which might be time-consuming and prone to errors. In contrast, the TOMAHAWK risk score comprises the summation of points.

Prognostic Risk Factors After Out-of-Hospital Cardiac Arrest

Most of the variables included in the TOMAHAWK risk score are established risk factors for mortality in OHCA patients. Importantly, the accurate time until ROSC might be difficult to ascertain from the emergency medical service at time of hospital admission and might be prone to imprecision. The TOMAHAWK risk score includes lactate levels as a predictor of mortality, which were the strongest mortality predictor. Although serial lactate measurements can be used as a marker for metabolic recovery in post-cardiac arrest patients and are likely superior for prognostication compared with a single measurement at admission, they can only be assessed over time and are therefore unsuitable for very early risk stratification (29, 30).

Although diabetes has been acknowledged as an important risk factor for sudden death in the 1990s (31), none of the previously mentioned risk scores included diabetes as an important risk factor. Apparently, none of the risk scores included any type of patient comorbidity as a prognostic risk factor. Interestingly, in the TOMAHAWK risk score, the impact of diabetes on prognosis was as strong as prolonged time to ROSC (≥ 23 min). These findings confirm the results of a systematic review and meta-analysis across seven studies with OHCA patients (32).

Based on the aforementioned risk factors, this study showed an incremental increase in mortality across risk categories, both in the TOMAHAWK development cohort, as well as in the COACT and Berlin cohorts. Furthermore, the risk score showed a good predictive performance for short-term mortality and a good calibration.

Limitations

This study contains limitations. First, the cohort size was smaller than some cohorts of other OHCA risk scores. Only patients without ST-segment elevations or hemodynamic/electrical instability at hospital admission were included, wherefore the TOMHAWK score might not be applicable to all OHCA patients. In particular, the exclusion of hemodynamically or electrically unstable patients, as well as those with presumed noncardiac etiologies of the arrest, may restrict its generalizability to more critically ill populations, such as those requiring immediate mechanical circulatory support or presenting with noncardiac causes. Second, complete-case analyses were performed after excluding patients with missing values in the risk score parameters. Imputation of missing values was not performed to avoid loss of risk score precision. Notably, patients who were excluded exhibited characteristics comparable to those who were included in the analysis, ruling out severe exclusion bias. Third, included medical centers were specialized in treating OHCA patients. The TOMAHAWK risk score might not be applicable to all levels of medical centers. Future validation efforts should focus on diverse healthcare settings, including rural hospitals, non-European hospitals, nonspecialized centers, facilities with varying resource levels and pre-hospital settings, to ensure the broader applicability of the TOMAHAWK score in real-world scenarios. Fourth, the COACT cohort included only patients with shockable initial electrocardiogram rhythms, a parameter incorporated in the TOMAHAWK score. This specific selection may explain the lower AUC observed in the COACT cohort during external validation. However, all patients in the COACT cohort were uniformly impacted by the absence of two score points. External validation was subsequently performed in the Berlin cohort (including shockable and unshockable arrest rhythms), which demonstrated improved diagnostic performance compared with the COACT cohort. Fifth, although the TOMAHAWK risk score was developed and validated using large multicenter cohorts, variations in data collection protocols and patient selection criteria across centers may impact its external applicability. Sixth, while this study focuses on 30-day mortality, future research should incorporate long-term outcomes, including health-related quality of life and functional status, to provide a more comprehensive understanding of patient trajectories following OHCA. Additionally, pre-hospital and dynamic risk assessment models incorporating serial lactate measurements could offer significant potential to enhance prognostic accuracy (30). While pre-hospital and/or serial lactate measurements were not performed in the TOMAHAWK trial, exploring the feasibility and utility of such models in future studies may provide valuable insights into the metabolic recovery and outcomes of post-arrest patients. Furthermore, withdrawal of life-sustaining therapy (WLST) may contribute to self-fulfilling prophecy bias in mortality predictions. Detailed data regarding the cause of death and WLST were not comprehensively collected for all patients in the TOMAHAWK trial. While this limitation is common in cardiac arrest research, it is essential to emphasize that the TOMAHAWK score should be used alongside clinical judgment and not as the sole factor in guiding care decisions.

CONCLUSIONS

The TOMAHAWK risk score is a simple, objective and practical tool to rapidly perform early prognostication of OHCA patients on hospital admission. The risk score could be used in clinical routine to support clinicians with defining therapy goals, adequately allocate healthcare resources, particularly in patients with poor prognosis, and standardize post-resuscitation medical care and cardiac arrest research.

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Dr. Thevathasan was involved in statistical analyses, investigation, article writing, and article review. Drs. Spoormans, Akin, Fuernau, Tebbe, Haeusler, Oeff, Hassager, Fichtlscherer, Zeymer, Pöss, Roßberg, Abdel-Wahab, Jobs, de Waha, Lemkes, Thiele, and Skurk were involved in investigation, resources, review of analyses, and article review. Dr. Freund was involved in investigation, review of analyses, and article review. Dr. Desch was involved in supervision, investigation, resources, article writing, and article review.

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The study was conducted according to the Declaration of Helsinki and was approved by the local ethics committees of each participating hospital. All patients or their legal representatives gave written informed consent.

The datasets generated and analyzed during the current study are not publicly available due patient privacy but are available from the corresponding author on reasonable request.

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