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Beyond screening for pulmonary arterial hypertension: The DETECT score is a potential promising prediction tool for all-cause mortality in systemic sclerosis: Analysis from the EUSTAR database

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ABSTRACT

Background: Systemic sclerosis (SSc) is characterized by an increased mortality. Various mortality risk factors are included in the DETECT algorithm, a screening tool for SSc-associated pulmonary arterial hypertension. We tested the DETECT score as a predictor of all-cause mortality in SSc.

Methods: SSc patients from the European Scleroderma Trial And Research (EUSTAR) cohort, with available data for calculating the DETECT and the SCOpE (currently proposed risk algorithm) scores and follow-up were included. Patients from the University Hospital Zurich served as derivation cohort, the remaining EUSTAR patients formed the validation cohort. Uni- and multivariable Cox regression tested the DETECT score as a predictor of mortality. A time-dependent ROC curve analysis was used to assess predictive accuracy (at 1, 3, and 5 years), and to derive and validate optimal cutoffs.

Results: The derivation cohort (n = 605) showed less cardio-pulmonary and diffuse cutaneous involvements, but longer follow-up and higher mortality than the validation cohort (n = 1017). The DETECT score independently predicted mortality in both cohorts, even after excluding pulmonary hypertension patients. Time-dependent ROC analysis showed excellent predictive accuracy for mortality (AUC>0.85) in the derivation cohort, non-inferior to the SCOpE score. In the validation cohort, a moderate-to-good performance for 1-year mortality was retained. A DETECT score>40 demonstrated strong performance (sensitivity≥0.68; specificity≥0.83) in the derivation, and performed moderately in the validation cohort (sensitivity = 0.54; specificity = 0.71).

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Conclusion: The DETECT score robustly predicts all-cause mortality in SSc across phenotypically different cohorts. A DETECT score>40 may refine risk stratification, guiding tighter monitoring and management. Further validation over 1-year outcomes is warranted.

1. Introduction

Systemic sclerosis (SSc) is a rare connective tissue disease associated with markedly increased mortality compared to the general population. Meta-analyses over the past two decades consistently report elevated standardized mortality ratios (SMRs) ranging from 2.7 to 3.6, with no significant decline over time [1,2]. This underscores the urgent need for robust yet practical tools to identify patients at high-risk. Accurate mortality prediction may not only guide treatment intensity and management decisions but also inform the design of clinical trials and novel therapeutic approaches.

SSc exhibits a wide spectrum of organ manifestations, many of which are key determinants of impaired survival [3]. Interstitial lung disease (ILD, 16.8%), pulmonary arterial hypertension (PAH, 14.7%), cancer (13.1%) and primary heart disease (12%) are among the most frequent causes of death in SSc [4]. The heterogeneity of SSc across patient populations and cohorts poses a major challenge in developing prognostic tools that are both comprehensive and broadly applicable in everyday clinical practice. This might be also true considering the change in available treatments over time, as newly approved, effective therapies might reduce the mortality specifically related to a single organ involvement. These changed survival patterns highlight the need to periodically renew the risk profile and develop new mortality prediction models. Currently, the SCleroderma mOrtality p EUSTAR (SCOpE) score represents the most robust, discriminative tool for predicting 3-year mortality in SSc (AUC 0.79, 95% CI 0.75–0.81) [4]. However, its reliance on 14 variables [i.e., age, male sex, diffuse cutaneous disease, history of scleroderma renal crisis, prominent dyspnea, digital ulcers, joint contractures, muscle weakness, elevated C-reactive protein, proteinuria, left ventricular ejection fraction <50%, ILD, diffusion capacity for carbon monoxide (DLCO)<60% predicted, and forced vital capacity (FVC) < 70% predicted] limits its practical use in daily clinical routine.

The DETECT score is a two-step screening algorithm for pulmonary arterial hypertension in SSc [5], currently recommended by international guidelines for annual use in SSc patients [6]. Most variables included in the DETECT score have been previously associated with mortality in SSc [4,7–18]. E.g. low FVC, a reduced DLCO, and elevated N-terminal pro-brain natriuretic peptide (NT-proBNP) levels are all risk factors for mortality and are also included in the DETECT score algorithm [4,5,10].

Therefore, we investigated the DETECT score as a predictive tool for all-cause mortality in SSc. We compared its predictive accuracy and discriminative performance with the established SCOpE score and determined optimal cutoff values for predicting 1-, 3-, and 5-year mortality.

2. Methods

2.1. Data source

SSc patients were first identified from the European Scleroderma Trial And Research (EUSTAR) cohort database (date of extraction March 14th 2025, approved as Clinical Project 170 by the EUSTAR board).

2.2. Study population and definitions

Patients were included in the study if they met the 2013 American College of Rheumatology (ACR)/European League Against Rheumatisms (EULAR) classification criteria [19], had available data to simultaneously calculate both the DETECT [5] and SCOpE [4] scores at least for one timepoint and survival information afterwards. For improved readability of the manuscript, we will use the term "DETECT" to indicate the final score after the calculation of the DETECT Step 2 score. The local EUSTAR cohort from University Hospital Zurich (EUSTAR Center 006) was used as the derivation cohort; the remaining EUSTAR cohort excluding Zurich patients, fulfilling the same inclusion criteria, constituted the validation cohort. Clinical, functional and laboratory parameters included in the analysis have been previously defined [20].

2.3. Outcome/Exposure

The primary endpoint was all-cause mortality. Observation started with the timepoint at which both the primary exposure of interest, namely the DETECT and SCOpE (comparator) scores could be calculated (defined as baseline visit). Patients were followed until death or last available timepoint with alive status.

2.4. Statistical analysis

Baseline characteristics were compared between derivation and validation cohorts, using two-sided *t*-test for continuous variables and chi-square test for categorical variables. Categorical variables are presented as absolute frequencies and corresponding percentages, and continuous variables are reported as mean values and standard deviations. The distribution of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation and were compared using parametric tests (Student's t-test), whereas non-normally distributed variables are reported as median (Q1-Q3) and analyzed using non-parametric tests (Mann–Whitney *U* test).

Given the high prevalence of missing data among the parameters required for the calculation of the DETECT and the SCOpE score, a complete-case approach was adopted. Only patients with available data required for the calculation of the DETECT and SCOpE scores and for the respective analyses were included. The extent of missing data for key variables was assessed, and no imputation was performed.

To test for potential collinearity between the DETECT and SCOpE scores, we used Spearman's correlation test, with collinearity defined as $r > |0.7|$. The predictive value of the DETECT score for overall mortality was first assessed at baseline visit using univariable Cox proportional hazards regression model and then adjusted for the SCOpE score as a confounder.

Given the expected, strong association between the DETECT score and the presence of any form of pulmonary hypertension (PH), as well as the known impact of PH on mortality in SSc, we conducted a sensitivity analysis excluding patients with PH, defined as a mean pulmonary arterial pressure (mPAP) > 20 mmHg on right heart catheterization (RHC) at any time point during follow-up (i.e., PH patients), as per recent international guideline documents [6]. Accordingly, PAH was additionally defined by a pulmonary wedge pressure ≤15 mmHg and pulmonary vascular resistances ≥2 wood units. An additional sensitivity analysis focused on 3-year mortality, as a reference duration of observation used during the development of the SCOpE score.

To evaluate the accuracy of the DETECT score in predicting mortality, a time-dependent ROC curve analysis was performed, estimating

predictive performance and defining optimal cut-off values for identifying high-risk patients at 1, 3, and 5 years. Stratification analyses were additionally implemented according to the skin subset (limited vs diffuse), age (below or above median value) and autoantibody subset (anticentromere, anti-topoisomerase I, others). To derive conservative cut-offs, patients with PH were excluded from this analysis. Cut-off values were selected in the derivation cohort based on a trade-off between sensitivity and specificity and were subsequently applied to the validation cohort.

Discriminative power was assessed by comparing the area under the time-dependent ROC curves (AUC) for the DETECT and SCOpE scores at 1, 3, and 5 years using the pointwise Z-test. Due to the limited follow-up duration in the validation cohort, the predictive value of the DETECT score and its derived cut-offs were validated using time-dependent ROC curve analysis at the 1-year time point only.

All statistical analyses were conducted using R (R Foundation for Statistical Computing, Vienna, Austria). The following R packages were utilized: *timeROC* for time-dependent ROC curve analysis, *survival* for survival analyses, *dplyr* and *tidyverse* for data manipulation and visualization, *survival* for time to conduct cox proportional hazard regression analysis, *psych* for descriptive and psychometric statistics and *ggplot2* for data visualization. A two-sided p-value <0.05 was considered statistically significant. Ethical approval for data collection and analysis was obtained from regional Ethics Committee, and the research was conducted in accordance with the Declaration of Helsinki. All data acquisition and analysis were performed following the STROBE guidelines [21].

3. Results

3.1. Study population, derivation and validation cohorts

The EUSTAR cohort database included 22,780 patients and was divided into a derivation cohort (821 patients, from University Hospital Zurich) and a validation cohort (21,959 patients; EUSTAR patients excluding those from Zurich). In the derivation cohort, 173 (21.1%) patients were excluded given insufficient data to calculate the DETECT or SCOpE scores, and additional 43 (5.2%) for missing follow-up information, resulting in 605 patients available for the study. In the validation cohort, after excluding 19,656 (92.9%) patients with missing data for either risk score at the same timepoint and 478 (2.3%) remaining patients due to missing follow-up information, 1017 patients were available for analysis. Supplementary Fig. 1 displays the availability of DETECT, SCOpE score and follow up data in SSc patients their distribution across the centers contributing to the EUSTAR cohort.

The derivation cohort was representative of a typical SSc population: 505 (83.5%) were female, 60 (9.9%) patients were diagnosed with PH, 259 (43%) had ILD and 122 (20%) had diffuse cutaneous disease. Overall, the mean DETECT and SCOpE scores at baseline were 33.7 ± 9.4 (with 130 points as a highest score reachable) and 6.8 ± 5.3 respectively (with 35 points as maximum possible score). Further information is reported in Table 1.

Compared to the derivation cohort, the validation cohort exhibited significantly higher disease burden, including higher prevalence of ILD (54% vs 43%, $p < 0.01$), PH (15 % vs 10%, $p = 0.01$) and diffuse cutaneous involvement (38% vs 20%, $p < 0.01$). Consistently, the mean scores for DETECT (36.7 vs 33.7, $p < 0.01$) and SCOpE (8.4 vs 6.8, $p < 0.01$) at baseline were significantly higher in the validation cohort compared to the derivation cohort (see Table 1).

Although a moderate correlation between DETECT and SCOpE-Score ($r = 0.570$, 95% CI 0.507 to 0.619) was detected, this did not meet our pre-defined threshold of collinearity.

3.2. Association of the DETECT score with mortality in the derivation cohort

Over a median follow up of 4.6 years (2.4-7.7) years, 82/605 (14%) patients from the derivation cohort died. The univariable Cox regression showed a positive association of the DETECT score with overall mortality (HR 1.09, 95%CI 1.07 to 1.10). When adjusted for the SCOpE score, the multivariable Cox regression model confirmed the DETECT score as an independent predictor for all-cause mortality over time (HR 1.05, 95% CI 1.03 to 1.07). Comparable results were obtained in the sensitivity analyses, when focusing on mortality at 3 years (35 deaths of 447 patients), and after excluding PH patients from the analysis (57 deaths of 545 patients) (Table 2).

The time-dependent ROC curves analysis showed optimal accuracy to identify mortality events for both the DETECT and the SCOpE scores, both with an AUC over 0.85 (Fig. 1). When comparing the two scores at the pre-defined timepoints, we observed no significant difference in discriminative power at 1 ($\Delta AUC = 0.02$, 95%CI -0.01 to 0.06), 3 ($\Delta AUC = 0.03$, 95%CI -0.02 to 0.09) and 5 years ($\Delta AUC = 0.04$, 95%CI -0.01 to 0.09). Additional analyses stratified by median age, antibody status, and cutaneous subtype showed similar, non-significantly different performance of the DETECT score compared to the SCOpE score. However, the DETECT score tended to perform less well in predicting mortality among younger patients and those who were ACA-positive, although both groups were characterized but very low number of deaths. Further details are provided in Fig. 1 and Supplementary Fig. 2–8. We observed that a DETECT score of 40 showed very good performance in predicting mortality at 1, 3 and 5 years (12, 33, 55 deaths at the three respective timepoints), both when including and excluding patients with PH. A DETECT score $\geq$40 consistently showed high rule-in performance, specifically a specificity $\geq$0.83 and NPV $\geq$0.95 at all assessed time points (1, 3, and 5 years) (see also Table 3).

3.3. Validation of the DETECT score as a predictor of mortality

In the univariable and adjusted analyses of the validation cohort, the DETECT score was confirmed as an independent predictor of overall mortality (univariable HR 1.07, 95 % CI 1.05 to 1.08; multivariable HR 1.04, 95 % C 1.02 to 1.06). In line with the derivation cohort, comparable results were maintained after excluding patients with PH (see Table 4). The three-year mortality sensitivity analysis could not be reliably assessed in the validation cohort, given the short mean follow-up of 2.5 years, with 60% of participants censored at timepoint 3 years, leaving the analysis underpowered.

Time-dependent ROC curve analysis at 1 year showed that both the DETECT and the SCOpE score had moderate-to-good accuracy in identifying deaths also in the validation cohort (AUC SCOpE = 0.81, AUC DETECT score = 0.71, $\Delta AUC = 0.1$, p-value 0.13; see Fig. 2). Applying the DETECT cutoff of 40 points in the validation cohort yielded moderate performance for 1-year mortality prediction, with sensitivity of 0.70, specificity of 0.71, a high NPV of 0.99, and a low PPV of 0.06. Excluding patients with PH produced comparable results, though with a slight drop in sensitivity (0.54), while specificity (0.75), PPV (0.04), and NPV (0.99) remained stable. Due to limited follow-up duration of the patients included in the validation cohort, no analysis at later timepoints could be performed.

4. Discussion

Our multicenter, longitudinal study suggests that the DETECT score may have utility as a prognostic marker for overall mortality in SSc, in addition to its established role as a screening tool for SSc-related PAH. Predictive performance was confirmed across two phenotypically distinct cohorts; however, in the validation cohort it could only be assessed for 1-year mortality and its performance was slightly reduced compared to the derivation cohort. Therefore, generalizability requires

further future validation. Importantly, we showed the predictive strength of the DETECT score was not driven by the presence of PAH or other classes of PH, neither by age, autoantibody status or subset of skin disease.

4.1. The DETECT score has face validity as a mortality prediction tool

The link between the DETECT score and mortality has multiple sources of strong face validity. Elhai et al. previously showed that PAH is among the most frequent causes of SSc-related deaths (14.7%) in the EUSTAR cohort, second only to ILD [4]. The DETECT algorithm is a high-sensitivity tool to identify patients with PAH, when applying a cut off of 35 points [5]. This means that the higher the DETECT score, the higher the likelihood of PAH and, consequently, higher risk of mortality. Although the prevalence of PAH was relatively low in both the derivation and validation cohorts, one might speculate that patients with increased DETECT score might represent a subgroup of patients with undiagnosed PH, given all possible limitations to the performance of RHC [5].

Recent studies show supportive data for an increased mortality risk associated with the individual components of the DETECT score, also beyond the contribution of PAH. For example, serum urate is a recognized marker of increased mortality across multiple conditions, including also SSc-PAH [7,8]. The lung function parameter DLCO is well known as a proxy for vascular lung involvement, but still a meaningful DLCO reduction can also reflect the presence of early ILD [22,23], in particular when associated with declined FVC. For this reason, both parameters are used to screen for and monitor ILD [9,24], as well as established determinants of poor survival in SSc [4,10]. Furthermore, the DETECT score might capture cardiac/myocardial involvement —another major contributor to mortality—through biomarkers such as NT-proBNP, right atrium area (RAA), tricuspid regurgitation velocity and changes in cardiac axis on electrocardiography [10,11,25]. In contrast to studies demonstrating associations between these parameters and mortality in SSc-PAH, evidence regarding the prognostic value of RAA and right axis deviation for all-cause mortality in SSc remains conflicting. One previous study could not find an association with increased overall mortality in SSc patients, though the study was probably underpowered for the assessing RAA as a risk factor [12]. Two cardiac magnetic resonance studies demonstrated that functional parameters associated with RA size, like reservoir and conduit strain, are predictors of all-cause mortality in SSc patients [18,26]. Right axis deviation is associated with increased overall mortality in patients with SSc who have established PH, but this has not been replicated yet in the broader SSc population without PH [10,27]. In addition to primary cardiac involvement (e.g., myocardial fibrosis and microvascular dysfunction) and cardiac disease secondary to PAH/PH in SSc [28], cardiovascular parameters included in the DETECT score may also capture broader cardiovascular disease, a very common causes of mortality in the general population [29]. To address this possibility and exclude secondary heart disease as a driver of mortality, more comprehensive cardiac assessment would be required, including RHC, cardiac magnetic resonance imaging, coronary artery evaluation, long-term ECG monitoring, and biopsystudies with detailed cardiac histological evaluation [25].

4.2. The DETECT score has face validity as a mortality prediction tool

The DETECT score was originally developed and validated as a screening instrument for SSc-PAH in a large multicenter trial and is still the most robust and accurate tool in identifying SSc patients at risk of PAH. Testing it outside this scope, we considered the SCOpE score, developed by the EUSTAR cohort, as the reference gold standard to predict mortality in SSc [4]. One could therefore anticipate that the DETECT score would perform worse than the SCOpE score, as the latter includes other important risk factors or causes of mortality, such as age, renal involvement, skin involvement, sex, as well as inflammatory biomarkers.

Contrary to this hypothesis, our data showed that the DETECT score had consistently high predictive accuracy for overall mortality at 1, 3,

Table 1
Demographics and clinical features of derivation and validation cohorts.

	n available	Derivation cohort	n available	Validation cohort	p-value
Sex (female), n (%)	605	505 (83.5%)	1017	856 (84.2%)	0.77
Age (years), mean ± SD	605	56.1 ± 14.5	1017	58.8 ± 13.3	<0.01
Follow up (years), median (Q1-Q3)	605	4.6 (2.4-7.7)	1017	2.2 (1-3.6)	<0.01
Disease duration (years), median (Q1-Q3)	588	6 (2.6-10.5)	1017	7.8 (3.8-15.1)	<0.01
PAPsys (mmHg), mean ± SD	581	27.1 ± 8.5	939	31.5 ± 19.9	<0.01
LVEF (%), mean ± SD	605	60.9 ± 5.1	1017	60.4 ± 6.3	0.06
DLCO (%), mean ± SD	605	73.5 ± 21.4	1017	62.7 ± 20.5	<0.01
FVC (%), mean ± SD	605	94.6 ± 19.7	1017	89.5 ± 22.1	<0.01
mRSS, median (Q1-Q3)	605	4.0 (0-6)	894	7.8 (2-12)	<0.01
CRP (mg/dl), mean ± SD	605	0.4 ± 1	1017	2.2 ± 8.6	<0.01
SCOpE score, mean ± SD	605	6.8 ± 5.3	1017	8.4 ± 4.7	<0.01
DETECT score, mean ± SD	605	33.7 ± 9.4	1017	36.7 ± 1	<0.01
Esophageal symptoms, n (%)	605	301 (49.8%)	1002	658 (64.7%)	<0.01
Intestinal symptoms, n (%)	604	194 (32.1%)	1008	251 (24.7%)	<0.01
Raynaud's phenomenon, n (%)	346	326 (94.2%)	168	161 (95.3%)	0.78
Digital ulcers (ever), n (%)	595	169 (27.9%)	974	473 (46.5%)	<0.01
SRC, n (%)	604	8 (1.3%)	1017	23 (2.3%)	0.25
PH, n (%)	605	60 (9.9%)	1017	152 (14.9%)	0.01
PAH, n (%)	605	41 (6.8%)	1017	101 (9.9%)	0.03
Joint involvement, n (%)	592	98 (16.0%)	993	98 (9.6%)	<0.01
Scl70 n (%)	599	147 (24.3%)	941	419 (41.2%)	<0.01
ACA n (%)	605	268 (44.3%)	1017	360 (35.4%)	<0.01
RNAPol3 n (%)	585	78 (12.9%)	959	58 (5.7%)	0.04
Diffuse skin subset, n (%)	599	122 (20.2%)	1016	381 (37.5%)	<0.01
ILD, n (%)	601	259 (42.8%)	1017	551 (54.2%)	<0.01
Mortality, n (%)	605	82 (13.6%)	1017	83 (8.2%)	<0.01

n: absolute number; FVC (%): predicted functional vital capacity (%); DLCO (%): Predicted Diffusing capacity for carbon monoxide (%); mRSS: modified Rodnan skin score; LVEF (%): left ventricular ejection fraction (%); PAPsys: systolic pulmonal arterial pressure; CRP: C- reactive protein; PH: pulmonary hypertension; PAH; pulmonary arterial hypertension, Scl70: anti-topoisomerase I antibody; ACA: anti-centromer antibodies; DETECT: DETECT step 2; ILD: interstitial lung disease; Mortality: all-cause mortality; RNAPol3: RNA polymerase III antibodies.

Table 2
Univariate and multivariate Cox proportional hazard regression analyses testing the DETECT score as predictor for overall mortality within the derivation cohort, including sensitivity analyses.

	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)	p-value
Derivation Cohort (n = 605, deaths = 82)				
DETECT	1.09 (1.07–1.10)	<0.01	1.05 (1.03–1.07)	<0.01
SCOpE	1.26 (1.21–1.30)	<0.01	1.20 (1.15–1.25)	<0.01
Derivation Cohort without PH (n = 545, deaths = 57)				
DETECT	1.09 (1.07–1.11)	<0.01	1.07 (1.04–1.09)	<0.01
SCOpE	1.26 (1.21–1.31)	<0.01	1.21 (1.16–1.27)	<0.01
Derivation Cohort – 3-Year Mortality (n = 447, deaths = 35)				
DETECT	1.08 (1.07–1.10)	<0.01	1.05 (1.03–1.08)	<0.01
SCOpE	1.28 (1.21–1.35)	<0.01	1.21 (1.13–1.28)	<0.01
Derivation Cohort without PH – 3-Year Mortality (n = 392, deaths = 23)				
DETECT	1.08 (1.06–1.10)	<0.01	1.06 (1.03–1.09)	<0.01
SCOpE	1.26 (1.19–1.34)	<0.01	1.21 (1.13–1.29)	<0.01

DETECT: DETECT step 2; HR: Hazard ratio; N: total number of patients; Mortality: all-cause mortality; PH: pulmonary hypertension.

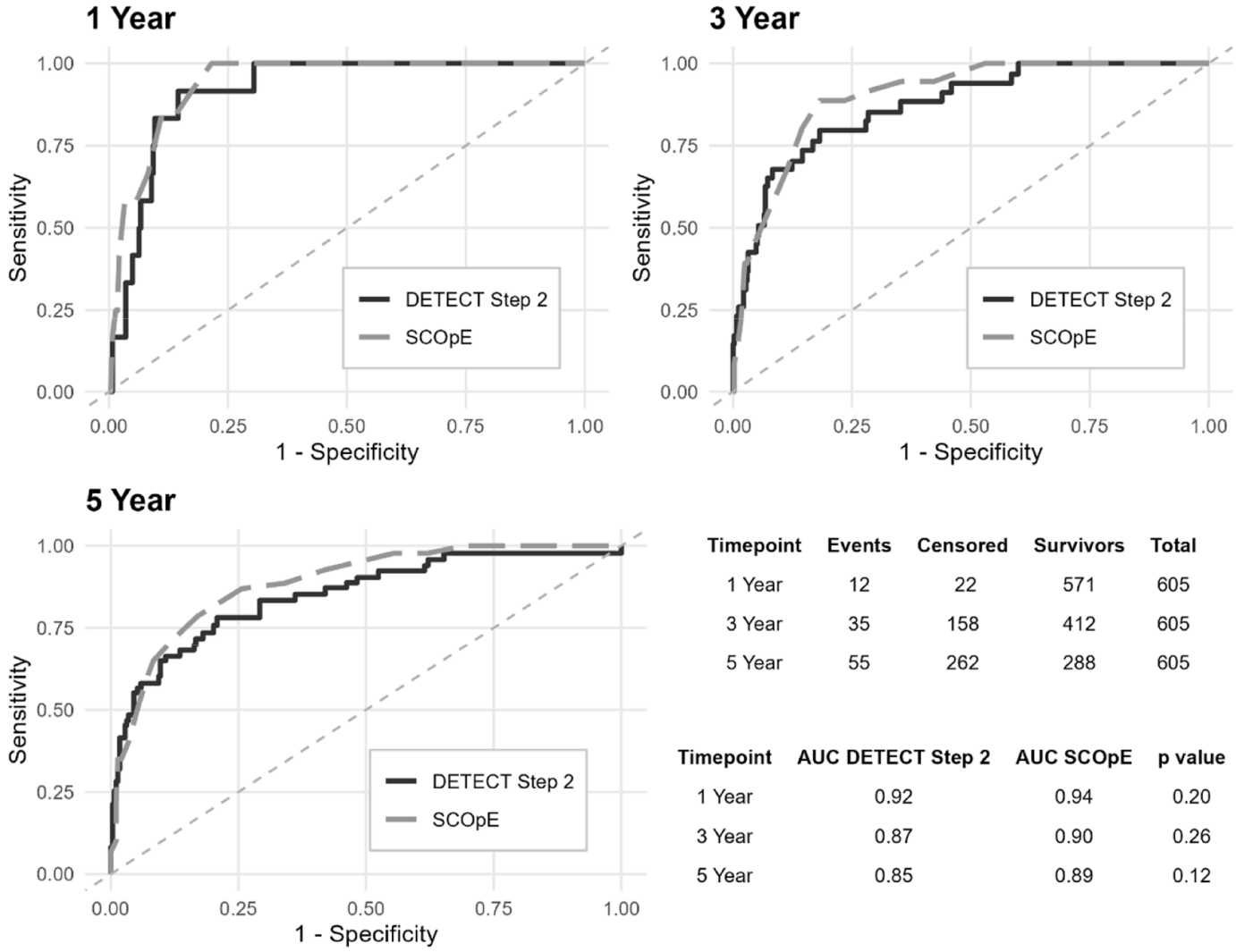
and 5 years in the derivation cohort, with performance comparable to the SCOpE score (ΔAUC $p > 0.05$ at all timepoints). When confirming our results in the validation cohort, the DETECT score showed a decrease in its predictive performance, although still not statistically significantly different from that of the SCOpE score (ΔAUC 0.10, $p = 0.13$).

Except for sex, all mortality risk factors included in the SCOpE score, but not covered in the DETECT score, were significantly more prevalent in the validation cohort, which might explain part of the tendency towards a lower prediction performance of DETECT vs SCOpE in the validation cohort.

Overall, these findings confirm the DETECT score is a well-performing and reproducible predictive tool for overall mortality in SSc, comparable and non-inferior to the SCOpE score. Additionally, the number of parameters required for its calculation, as well as its routine acquisition for screening purposes, support higher feasibility of DETECT compared to the SCOpE score.

4.3. Strengths and limitations

The major strengths of our study are the high standards of data collection and longitudinal follow-up. This is particularly true in the derivation cohort, where approximately 75% of the patients could be included in the analysis because of having both the information required for the risk scores calculation and the follow-up information. Since the availability of the data for the DETECT calculation was an inclusion



Timepoint	Events	Censored	Survivors	Total
1 Year	12	22	571	605
3 Year	35	158	412	605
5 Year	55	262	288	605

Timepoint	AUC DETECT Step 2	AUC SCOpE	p value
1 Year	0.92	0.94	0.20
3 Year	0.87	0.90	0.26
5 Year	0.85	0.89	0.12

Fig. 1. Time-dependent ROC Curve analysis in the derivation cohort. Comparing predictive accuracy of DETECT Step 2 and SCOpE scores for mortality in the derivation cohort using time dependent ROC-Curves at timepoints 1, 3 and 5 years. AUC: area under the curve. The reported p-values refer to pointwise Z-tests assessing differences between the DETECT and SCOpE AUCs at each timepoint.

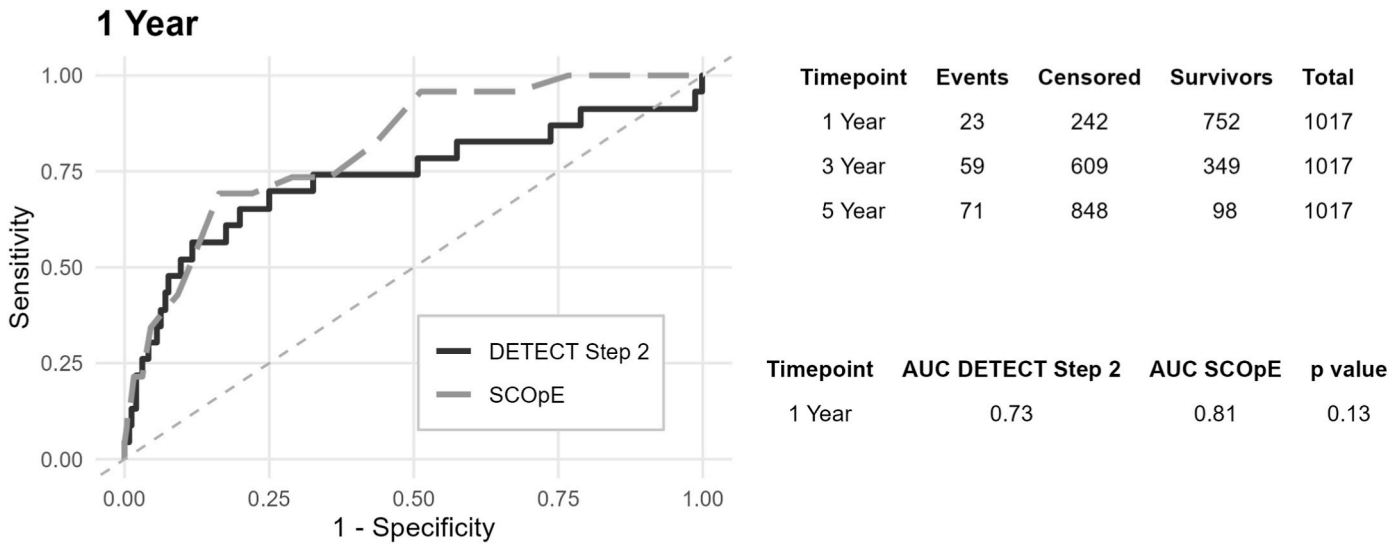


Fig. 2. Time-dependent ROC Curve analysis in the validation cohort. Comparing predictive accuracy of DETECT Step 2 scores and SCOpE Score for mortality in the validation cohort using time dependent ROC-Curves at timepoint 1 year. AUC: area under the curve. The reported p-value refers to the pointwise Z-test assessing the difference between the DETECT and SCOpE AUCs.

Table 3
Predictive accuracy for DETECT Cutoff = 40 in the derivation cohort for all-cause mortality.

Time (Years)	Sensitivity (Incl/Excl PH)	Specificity (Incl/Excl PH)	PPV (Incl/Excl PH)	NPV (Incl/Excl PH)
1	0.92/0.87	0.83/0.88	0.10/0.10	1.00/1.00
3	0.74/0.65	0.85/0.91	0.26/0.27	0.98/0.98
5	0.68/0.59	0.87/0.91	0.40/0.40	0.95/0.96

DETECT: DETECT step 2; Excl.: Excluding; Incl: Including; NPV: negative predictive value; PH: pulmonary hypertension; PPV: positive predictive value.

Table 4
Association of DETECT and SCOpE scores with mortality over time in the validation cohort.

	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)	p-value
Validation Cohort (n = 1017, all-cause deaths = 83)				
DETECT	1.07 (1.05–1.08)	<0.01	1.04 (1.02–1.06)	<0.01
SCOpE	1.22 (1.16–1.27)	<0.01	1.18 (1.12–1.24)	<0.01
Validation Cohort without PH (n = 865, all-cause deaths = 58)				
DETECT	1.07 (1.04–1.10)	<0.01	1.03 (1.01–1.07)	0.02
SCOpE	1.24 (1.17–1.30)	<0.01	1.21 (1.14–1.28)	<0.01

DETECT: DETECT step 2; HR: Hazard ratio; N: total number of patients; PH: pulmonal hypertension.

criterion of our study, one could argue that this leads to a selection bias and creating a study population with overrepresentation of patients at high risk of, or with high prevalence of PAH, therefore driving predictive performance for mortality of the DETECT score. However, the local cohort at University Hospital Zurich is getting routine annual assessments, including DETECT calculation for PAH risk stratification for every patient as per current international guidelines [6]. This systematic approach reduces selection bias. Furthermore, the proportion of PH in our derivation cohort aligns with published prevalence rates, suggesting representativeness despite exclusion of patients with insufficient follow-up. However, the selection bias might be an issue in our validation cohort, which only included around 5 % of the EUSTAR cohort, due to the lack of data needed to calculate the DETECT/SCOpE scores. The lower number of available DETECT scores in the EUSTAR cohort may be explained by the fact that the recommendation introduced in the 2022 ESC/ERS PAH guidelines is still being implemented. In contrast, the Department of Rheumatology at University Hospital Zurich participated in the development study of the DETECT score and has been applying it routinely since its initial publication. The 1017 patients of the validation cohort were recruited from 68 centers, with a median contribution of 6 patients per centre (range 1–117) (Supplementary Fig. 1), suggesting some degree of center dependence. However, no single center appears to dominate the dataset, and feasibility of a center-level analysis is not given. Additionally, the predictive value of DETECT score for mortality could only be assessed for 1-year mortality in the validation cohort, due to a notably shorter follow-up duration compared to the derivation sample. Further validation over the next future is expected to address both the limited sample size and the relatively short follow-up. Despite this, the DETECT model also performed moderately well in the EUSTAR validation cohort, which displayed higher disease burden and heterogeneity in organ manifestations, compared to the derivation cohort. Although possible, we do not believe that the reduced performance of the DETECT score in the validation cohort is primarily attributable to the higher disease burden, but rather to the nature of the subset of EUSTAR data analyzed. Notably, despite a higher disease burden and longer disease duration, the validation cohort exhibited unexpectedly lower mortality rates, suggesting potential underreporting of mortality. As the SCOpE score was developed within the EUSTAR cohort, including these patients, it is less susceptible to such cohort-specific limitations.

In conclusion, our findings support the DETECT score as a potential predictive tool for overall mortality in SSc. This unifies two important clinical assessments— i.e., risk stratification for PAH and for overall mortality — into a single risk score, simplifying the already complex evaluation of patients with SSc. A DETECT score greater than 40 points identified with a high specificity patients at high risk of mortality and thus might indicate the need to intensify or change management strategies, including careful reassessment of organ involvement and closer clinical follow-up. Future studies should validate the predictive performance of the DETECT score for long term mortality (>1 years), and evaluate its predictive performance for specific causes of mortality, including both SSc-related and non-related events, potentially enabling individualized risk prediction and management strategies.

CRediT authorship contribution statement

Florian Käs: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis,

Data curation. **Muriel Elhai:** Writing – review & editing. **Mike O. Becker:** Writing – review & editing. **Rucsandra Dobrota:** Writing – review & editing. **Carina Mihai:** Writing – review & editing. **Gesa Sauer:** Writing – review & editing. **Lorenzo Tofani:** Formal analysis. **Radim Bečvář:** Writing – review & editing. **Simona Rednic:** Writing – review & editing. **Patricia E. Carreira:** Writing – review & editing. **Gábor Kumánovics:** Writing – review & editing. **Paolo Airò:** Writing – review & editing. **Ulf Mueller-Ladner:** Writing – review & editing, Conceptualization. **Francesco Del Galdo:** Writing – review & editing. **Ana-Maria Ramazan:** Writing – review & editing. **Mickaël Martin:** Writing – review & editing. **Carmen-Pilar Simeón-Aznar:** Writing – review & editing. **Magda Parvu:** Writing – review & editing. **Nicoletta Del Papa:** Writing – review & editing. **Anna-Maria Hoffmann-Vold:** Writing – review & editing. **Oliver Distler:** Writing – review & editing. **Cosimo Bruni:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of generative AI use

No generative AI tools were used to generate original research data, analyses, results, or figures. During the preparation of this manuscript, the authors used ChatGPT (OpenAI) and OpenEvidence to improve the clarity and readability of the text and to support a thorough, manual literature search to identify relevant scientific literature. These tools were used to assist with language refinement and the exploration of existing evidence, but not as a substitute for the authors' own critical analysis, interpretation, or scientific judgment. All AI-assisted outputs were carefully reviewed, verified, and edited by the authors to ensure accuracy, completeness, and originality. The authors take full responsibility for the content of the published article, including the verification of cited sources and the integrity of the conclusions.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: **Muriel Elhai** reports a relationship with Boehringer Ingelheim that includes: consulting or advisory and funding grants. Muriel Elhai reports a relationship with Vontobel Stiftung that includes: funding grants. Muriel Elhai reports a relationship with Pfizer that includes: funding grants. Muriel Elhai reports a relationship with Novartis Foundation for Bio-Medical Research that includes: funding grants. Muriel Elhai reports a relationship with Iten Kohaut Foundation that includes: funding grants. Muriel Elhai reports a relationship with Kurt und Senta Herrmann Foundation that includes: funding grants. Muriel Elhai reports a relationship with Foundation for Research in Rheumatology (FOREUM) that includes: funding grants. Muriel Elhai reports a relationship with University Zurich that includes: funding grants. 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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaut.2026.103555.

Data availability

Anonymized data might be available from OD at the Department of Rheumatology, University Hospital Zurich, University of Zurich, Switzerland on reasonable request.

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