Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

American Journal of Emergency Medicine 57 (2022) 230–233

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Predictivity of frontal QRS-T angle for death in COVID-19 patients may differ by age

To the Editor,

The frontal QRS-T angle (fQRS-T angle), a measure easily derived from a 12-lead-electrocardiogram (ECG), approximates the angle between the vectors of depolarization and repolarization. Alterations in the fQRS-T angle may be related to myocardial abnormalities and its prognostic utility in predicting cardiac arrest or cardiac death was suggested [1-5]. We were intrigued when we read that the fQRS-T angle can be used as a reproducible, inexpensive, new, and powerful predictor in determining the clinical severity and prognosis of COVID-19 patients [6]. However, the results of this study merit being reproduced in a larger population of patients. Moreover, these results are not transferable to all patients because the mean patient age was restricted to 53 ± 12 years.

Between 27 March 2020 and 16 June 2021, a total of 309 consecutive patients with acute SARS-CoV-2 infection were admitted at the Infectious and Tropical Disease Unit of the "Mater-Domini" Teaching Hospital, Catanzaro, Italy, and were retrospectively included in the present study. Description of a part of this cohort and prediction of the clinical outcome was already reported [7].

In addition to the parameters that were already analyzed, all participants underwent 12-lead-ECG testing. The ECGs were read and interpreted by trained specialists who measured the QT-interval, QRS-axis, and T-wave-axis according to guidelines [8]. The fQRS-T angle was calculated as the smallest angle between the frontal plane QRS and T-wave axes (QRS-T angle = |QRS-axis–T-wave-axis|; if |QRS-T angle| was >180°, complimentary angle [360° − angle] was used) [3].

Statistical analysis was performed with IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). The participants were divided into two groups according to the fQRS-T angle tertiles: the higher tertile group with fQRS-T angle >50° and <180° (103 participants), and the lower tertile group with fQRS-T angle >0° and ≤50° (206 participants). The values were expressed as frequencies or mean ± standard deviation. Survival analysis was conducted with log-rank test and Kaplan-Meier curves. Univariate and multivariable Cox regression analyses along with calculation of the Hazard Ratio (HR) was done to determine if the fQRS-T angle could be an independent risk factor for 30-day mortality. A sensitivity analysis was conducted to stratify the population into two groups by age: <75 years and ≥75 years (highest tertile) to assess whether the correlation of fQRS-T angle with in-hospital mortality could have been diluted in the aging population because of multiple co-morbidities in this sub-population having an impact on the risk of death [8].

The characteristics of the 309 patients are described in Table 1.

The mortality rate was higher in the group of patients with fQRS-T angle >50° and <180° (23.2% vs. 7.8%). Furthermore, patients who died had a wider fQRS-T angle (76.1 ± 52.5°) when compared to the survivors (43.9 ± 42.4°). Kaplan-Meier survival curves also revealed significantly greater mortality at 30 days in the group of patients with fQRS-T angle >50° and <180° (Fig. 1). The Cox regression model showed that participants with fQRS-T angle >50° and <180° (24 of 103 participants) had a significant HR = 2.97 (95% CI, 1.57–5.16) for mortality compared to participants with fQRS-T angle >0° and ≤50° (16 of 206 participants). However, after adjusting for age, sex, arterial hypertension, atrial fibrillation, chronic obstructive pulmonary disease, and chronic kidney disease), this result was no longer significant (Table 2). Therefore, the population was stratified by age, using a predefined cut-off of 75 years. Results of the Cox regression showed that only in participants with age <75 years, fQRS-T angle >50° and <180° was significantly associated with in-hospital mortality both in univariate (HR = 7.29 [95% CI, 2.18–24.34] and multivariable (adjusted for the above-reported variables, besides age) analyses [HR = 8.72 (95% CI, 1.77–42.86)].

Our results confirm the correlation between fQRS-T angle and mortality in COVID-19 patients [6]. The patients who died had a greater fQRS-T angle than those who survived. Interestingly, while this correlation was strong and independent in patients with an age <75 years, it was not confirmed in individuals with age >75 years, probably due to a diluting effect exerted by other factors which were more prevalent in older individuals.

From the pathophysiological point of view, in SARS-CoV-2 disease there is cardiovascular involvement (cytokine storm, hypoxic damage, electrolyte abnormalities, plaque rupture, coronary spasm, microthrombi, endothelial lesions, direct myocardial injury) which can lead to a worsening of normal ventricular repolarization, thus increasing the angle between depolarization and repolarization and exposing the patient to a greater risk of mortality. Therefore, the fQRS-T angle could represent an added value to the clinical stratification, considering that the nature of a final event is always multifactorial and never the result of a single predictor. The fQRS-T angle measured on an ECG is a cost-effective method and could be a valuable predictor of mortality. More powerful studies should clarify whether this prediction can differ in subpopulations of patients according to age and/or co-morbidities associated with aging.

https://doi.org/10.1016/j.ajem.2022.02.051

Table 1
Clinical, anthropometric, biochemical and electrocardiographic characteristics of patients with COVID-19.

Variables	All Patients (n° 309)	Frontal QRS-T angle ≥0° e ≤50° (n° 206)	Frontal QRS-T angle >50° e ≤180° (n° 103)	*p*
Age (years)	67 ± 15.5	63.6 ± 14.9	73.8 ± 14.3	*0.0001*
Male sex	167 (54%)	111 (53.9%)	56 (54.4%)	0.936
LOS (days)	15.1 ± 10.2	15 ± 10.7	15 ± 9.2	0.931
Death	40 (12.9%)	16 (7.8%)	24 (23.3%)	*0.0001*
Cancer	20 (6.5%)	10 (4.9%)	10 (9.7%)	0.102
Hypertension	185 (59.9%)	110 (53.4%)	75 (72.8%)	*0.0001*
Chronic coronary disease	23 (7.4%)	13 (7.2%)	10 (12.3%)	0.177
Heart failure	11 (3.6%)	6 (3.3%)	5 (6.2%)	0.282
Atrial fibrillation	21 (6.8%)	3 (1.6%)	18 (22.2%)	*0.0001*
Stroke	4 (1.3%)	2 (1.1%)	2 (2.4%)	0.313
Diabetes mellitus	71 (23%)	42 (20.4%)	29 (28.2%)	0.126
COPD	34 (11%)	17 (8.3%)	17 (16.5%)	*0.029*
Asthma	10 (3.2%)	6 (3.3%)	4 (4.9%)	0.528
CKD	41 (13.3%)	16 (7.8%)	25 (24.3%)	*0.0001*
Obesity	100 (32.4%)	70 (34%)	30 (29%)	0.390
Polipharmacy	173 (56%)	101 (49%)	72 (70.6%)	*0.0001*
ACE-i	70 (22.7%)	37 (18%)	33 (32.4%)	*0.0005*
ARBs	69 (22.3%)	44 (21.4%)	25 (24.5%)	0.553
Statins	67 (21.7%)	42 (20.6%)	25 (24.5%)	0.434
Diuretics	76 (24.6%)	44 (21.4%)	32 (32.1%)	0.058
Acetylsalicylic acid	63 (20.4%)	37 (20.1%)	26 (32.1%)	*0.035*
DOAC	11 (3.6%)	5 (2.7%)	6 (7.4%)	0.078
β-blockers	72 (23.3%)	38 (20.7%)	34 (42%)	*0.0001*
SBP (mmHg)	132.8 ± 20.1	133.4 ± 19.6	131.5 ± 21.1	0.437
DBP (mmHg)	76.5 ± 12.3	77.3 ± 11.6	74.8 ± 13.6	0.086
HR (bpm)	81.2 ± 14.5	80.6 ± 14.1	82.6 ± 15.2	0.238
SpO2 (%)	93.8 ± 5.5	93.8 ± 5.7	93.6 ± 5.1	0.733
P/F	248.8 ± 113.5	248.5 ± 105.6	249.6 ± 129.4	0.944
Temperature (°C)	36.3 ± 0.6	36.4 ± 0.6	36.2 ± 0.5	*0.028*
BMI (Kg/m^2)	28.7 ± 5.4	28.7 ± 5.6	25.7 ± 4.9	0.990
QT (msec)	369.6 ± 42.1	368.3 ± 41.6	372.4 ± 43.1	0.428
QTc (msec)	421.9 ± 33.7	419.5 ± 31.2	427.2 ± 38.2	0.070
Frontal ARS-T angle (°)	48.1 ± 45.1	43.9 ± 42.4	76.1 ± 52.5	*0.0001*
eGFR (ml/min x$1.73m^2$)	90.8 ± 44.8	98.6 ± 47	74.9 ± 35.3	*0.0001*
Creatinine (mg/dl)	1.06 ± 0.95	1 ± 0.95	1.18 ± 0.95	0.131
Aspartate transaminase (UI/L)	38.8 ± 71.6	34.5 ± 22.8	47.4 ± 119.4	0.137
Alanine transaminase (UI/L)	37.2 ± 93.4	34.8 ± 30.3	42.1 ± 156.7	0.521
Interleukin-6 (pg/ml)	62.2 ± 216.2	48.5 ± 182.3	89.4 ± 270.1	0.125
Fibrinogen (mg/dl)	520 ± 128.8	527.4 ± 126.2	505.3 ± 133.1	0.166
Sodium (mmol/L)	138.1 ± 8.8	138.1 ± 10.1	138.2 ± 5.1	0.938
Potassium (mmol/L)	4 ± 0.6	4 ± 0.5	3.9 ± 0.6	0.720
Ferritin level (ng/ml)	792.1 ± 735.2	817.4 ± 749.8	740.9 ± 705.9	0.405
Lactate dehydrogenase (U/L)	468.3 ± 237.9	442.2 ± 211.9	519.5 ± 276.1	*0.007*
Albumin (g/dl)	3.8 ± 2.1	3.8 ± 2.5	3.6 ± 0.4	0.459
Uric acid (mg/dl)	5 ± 1.8	4.7 ± 1.5	5.7 ± 2.1	*0.0001*
LDL cholesterol (mg/dl)	86.7 ± 32.2	89.9 ± 32.9	79.6 ± 29.4	*0.041*
Creatine phosphokinase (UI/L)	188.9 ± 323.1	173 ± 296.3	224.1 ± 375	0.244
Hemoglobin (g/dl)	13.2 ± 2.9	13.2 ± 3.3	13 ± 1.9	0.472
Lymphocytes count (x10^3/uL)	1329.1 ± 5789.3	1520.5 ± 7061	942.5 ± 536.8	0.413
C reactive protein (mg/L)	63.3 ± 59.7	59.2 ± 56.9	71.4 ± 64.6	0.101
D-dimer (mg/L)	1.9 ± 4.3	1.27 ± 2.3	3.1 ± 6.4	*0.0001*

nLOS. lenght of stay; COPD. chronic obstructive pulmonary disease; CKD. chronic kidney disease; ACE-i. Angiotensin-converting enzyme inhibitors; ARBs. angiotensin receptor blocker; DOAC. direct-acting oral anticoagulants; SBP. systolic blood pressure; DBP. diastolic blood pressure; HR. hert rate; SO2. oxygen saturation; BMI. body mass index; eGFR. estimated glomerular Data are expressed as mean + SD. number (percentage).
Student's t-test for continuous variables and the analysis of $\chi 2$ (Chi-square) for qualitative variables. Significance: $p < 0.05$.

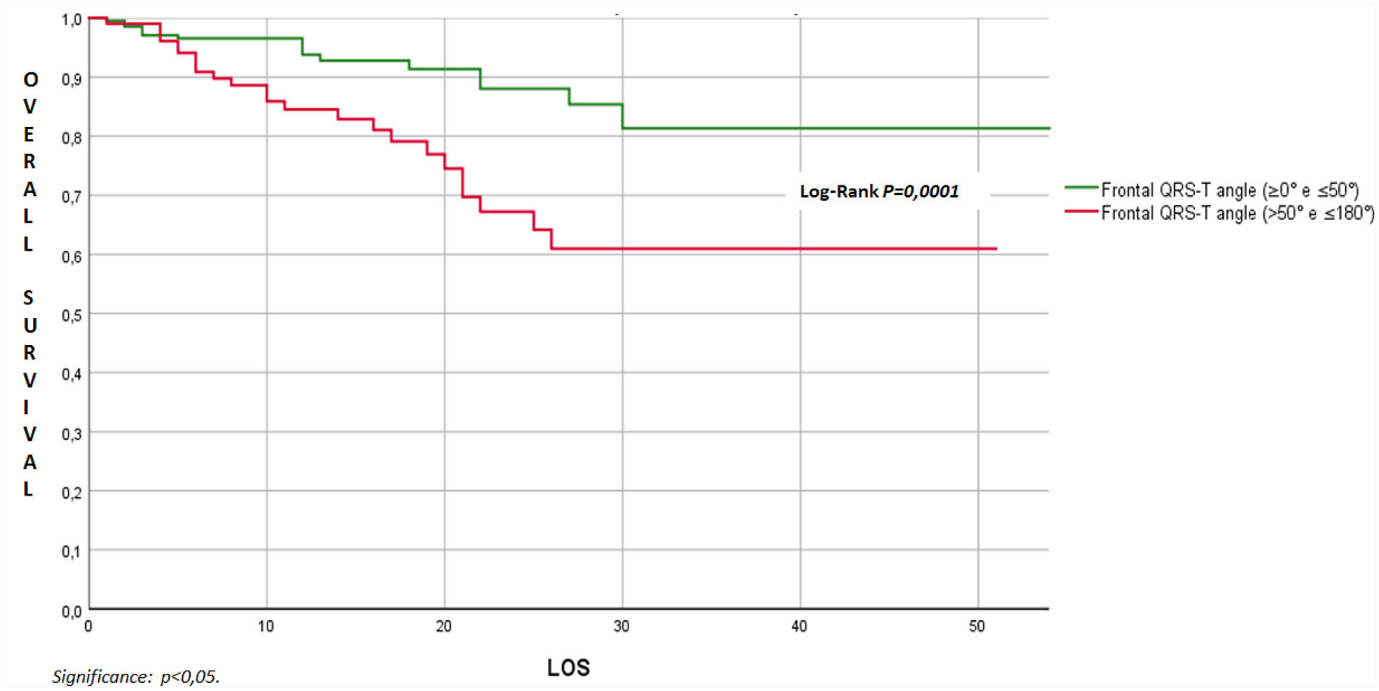

Fig. 1. Kaplan-Meier survival curves by frontal ARS-T angle group.

Table 2
Cox regression analysis

	Event rate	*HR*	*95% CI*	*P*	Multivariated adjusted*		
					HR	*95% CI*	*P*
Frontal QRS-T angle ≥0° e ≤50°	16/206 (7.8%)	–	–	–	—	—	—
Frontal QRS-T angle >50° e ≤180°	24/103 (23.3%)	2.97	1.57-5.16	*0.001*	1.63	0.66-4.00	0.284

CI. Confidence interval; HR. hazard ratio.
* Multivariate model adjusted for age. sex. hypertension. atrial fibrillation. COPD. CKD. Significance: $p < 0.05$.

Credit authorship contribution statement

Bruno Tassone: Writing – original draft, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Enrico Maria Trecarichi:** Writing – review & editing, Validation, Supervision, Formal analysis, Data curation, Conceptualization. **Carlo Torti:** Writing – review & editing, Supervision, Resources, Investigation, Conceptualization.

Declaration of Competing Interest

None.

References

[1] Kardys I, Kors JA, van der Meer IM, Hofman A, van der Kuip DA, Witteman JC. Spatial QRS-T angle predicts cardiac death in a general population. Eur Heart J. 2003;24:1357–64. [PubMed: 12871693].
[2] Zhang ZM, Prineas RJ, Case D, Soliman EZ, Rautaharju PM, Group AR. Comparison of the prognostic significance of the electrocardiographic QRS/T angles in predicting incident coronary heart disease and total mortality (from the atherosclerosis risk in communities study). Am J Cardiol. 2007;100:844–9. [PubMed: 17719331].
[3] Yamazaki T, Froelicher VF, Myers J, Chun S, Wang P. Spatial QRS-T angle predicts cardiac death in a clinical population. Heart Rhythm. 2005;2:73–8. [PubMed: 15851268].
[4] Pavri BB, Hillis MB, Subacius H, Brumberg GE, Schaechter A, Levine JH, et al. Prognostic value and temporal behavior of the planar QRS-T angle in patients with nonischemic cardiomyopathy. Circulation. 2008;117:3181–6. [PubMed: 18574059].
[5] Rautaharju PM, Kooperberg C, Larson JC, LaCroix A. Electrocardiographic predictors of incident congestive heart failure and all-cause mortality in postmenopausal women: the Women's Health Initiative. Circulation. 2006;113:481–9. [PubMed: 16449727].
[6] A new predictor for indicating clinical severity and prognosis in COVID-19 patients: frontal QRS-T angle. Metin Ocak, Mustafa Begenc Tascanov, Nur Şimşek yurt, Yusuf can yurt. Am J Emerg Med. 2021 Dec. https://doi.org/10.1016/j.ajem.2021.09.046.
[7] Trecarichi Enrico Maria, Mazzitelli Maria, Serapide Francesca, Pelle Maria Chiara, Tassone Bruno, Arrighi Eugenio, et al. Clinical characteristics and predictors of mortality associated with COVID-19 in elderly patients from a long-term care facility. Sci Report. 2020. https://doi.org/10.1038/s41598-020-77641-7. Published: 30 November 2020. Article number: 20834.
[8] Surawicz B, Childers R, Deal BJ, Gettes LS, Bailey JJ, Gorgels A, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association electrocardiography and arrhythmias committee, council on clinical cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. Circulation. 2009;119:e235–40. [PubMed: 19228822].

Bruno Tassone*
Azienda Ospedaliero-Universitaria Mater Domini, University Magna Graecia, 88100 Catanzaro, Italy
*Corresponding author.
E-mail address: bruno.tassone2@studenti.unicz.it

Marco Ricchio
Azienda Ospedaliero-Universitaria Mater Domini, University Magna Graecia, 88100 Catanzaro, Italy

Francesca Serapide
Azienda Ospedaliero-Universitaria Mater Domini, University Magna Graecia, 88100 Catanzaro, Italy

Rosaria Lionello
Azienda Ospedaliero-Universitaria Mater Domini, University Magna Graecia, 88100 Catanzaro, Italy

Enrico Maria Trecarichi
Azienda Ospedaliero-Universitaria Mater Domini, University Magna Graecia, 88100 Catanzaro, Italy

Carlo Torti
Azienda Ospedaliero-Universitaria Mater Domini, University Magna Graecia, 88100 Catanzaro, Italy