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Cardiac CT and MRI radiomics: systematic review of the literature and radiomics quality score assessment

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Abstract

Objective To systematically review and evaluate the methodological quality of studies using magnetic resonance imaging (MRI) and computed tomography (CT) radiomics for cardiac applications.

Methods Multiple medical literature archives (PubMed, Web of Science, and EMBASE) were systematically searched to retrieve original studies focused on cardiac MRI and CT radiomics applications. Two researchers in consensus assessed each investigation using the radiomics quality score (RQS). Subgroup analyses were performed to assess whether the total RQS varied according to study aim, journal quartile, imaging modality, and first author category.

Results From a total of 1961 items, 53 articles were finally included in the analysis. Overall, the studies reached a median total RQS of 7 (IQR, 4–12), corresponding to a percentage score of 19.4% (IQR, 11.1–33.3%). Item scores were particularly low due to lack of prospective design, cost-effectiveness analysis, and open science. Median RQS percentage score was significantly higher in papers where the first author was a medical doctor and in those published on first quartile journals.

Conclusions The overall methodological quality of radiomics studies in cardiac MRI and CT is still lacking. A higher degree of standardization of the radiomics workflow and higher publication standards for studies are required to allow its translation into clinical practice.

Key Points

- *RQS has been recently proposed for the overall assessment of the methodological quality of radiomics-based studies.*
- *The 53 included studies on cardiac MRI and CT radiomics applications reached a median total RQS of 7 (IQR, 4–12), corresponding to a percentage of 19.4% (IQR, 11.1–33.3%).*
- *A more standardized methodology in the radiomics workflow is needed, especially in terms of study design, validation, and open science, in order to translate the results to clinical applications.*

Keywords Systematic review · Cardiovascular system · Magnetic resonance imaging · Multidetector computed tomography

Abbreviations

CT	Computed tomography
IQR	Interquartile range
MRI	Magnetic resonance imaging
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
PROSPERO	International Prospective Register of Systematic Reviews
RQS	Radiomics quality score

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Introduction

Radiomics is an emerging research field aimed to improve diagnosis, characterization, and prognosis by automated or semi-automated quantitative analysis of medical images [1]. Although it is often applied in oncologic research to extract information concerning tumor features [2], there is an increasing interest in its usage for cardiac imaging [3,

4]. Currently, cardiovascular diseases represent the main cause of morbidity and mortality worldwide [5], leading to an ongoing clinical demand for improvements in diagnostic accuracy and patient risk stratification by using non-invasive diagnostic techniques [6, 7]. Therefore, new imaging biomarkers identified by data extraction from cardiac computed tomography (CT) and magnetic resonance imaging (MRI) may be beneficial for the assessment of several pathologies, such as atherosclerotic coronary artery disease, myocardial viability, and cardiomyopathies [8, 9]. Despite the great potential of radiomics and its increasing application in cardiac imaging [10–13], the role of data-driven biomarkers in clinical practice remains still underexploited mainly due to the intrinsic complexity of the method and the poor reproducibility of the high number of processes involved, including image acquisition, preprocessing, segmentation, feature extraction, and dataset analysis [14, 15]. Indeed, these aspects represent a widespread limiting factor and reinforce the need to standardize data collection, evaluation criteria, and reporting of radiomic workflows. For this purpose, the radiomics quality score (RQS) has been recently proposed for the overall assessment of the methodological quality of radiomics-based studies and especially employed in the oncologic field [14, 16–19]. The aim of our systematic review was to evaluate the methodological quality of studies published on cardiac MRI and CT radiomics applications for multiple purposes.

Methods

Protocol and registry

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [20]. The review protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO, registration number = CRD42021237948).

Search strategy

Two investigators (A.P. and A.S.) conducted a systematic search of all studies using radiomics in cardiac MRI and/or CT exams on multiple electronic databases (Pubmed, Scopus, and Web of Science) published up to February 7, 2021. The following search terms and their variations were used: "radiomics" AND "cardiac" AND "computed tomography" OR "magnetic resonance"; the detailed search string is available in the supplementary materials. After removal of duplicates, abstracts were screened in order to remove papers that did not present original research (e.g., reviews, editorials, case reports), not focused on the topic of interest, published in languages other than English, or not involving human subjects. Moreover, the reference lists of the included papers were also screened to find potentially eligible studies missed in the primary search.

Data collection and study evaluation

The RQS was used to assess the methodological quality of included studies [14]. In detail, it comprises the assessment of 16 items regarding various steps in the workflow of radiomics analysis such as imaging protocol, feature extraction, data modeling, model validation, and data sharing. The summed total score ranges from − 8 to 36 that is converted into a final 0–100 percentage score (Table 1). Two readers (R.C. and A.S.) evaluated the papers in consensus. Both raters had previous experience in RQS assessment with good to moderate inter-reader reproducibility [14, 21].

Statistical analysis

The Shapiro–Wilk test was used to assess the normality of distribution for continuous variables. These are presented as median and interquartile range (IQR) while categorical data as counts and percentages. Subgroup analyses were performed to assess whether the total RQS varied significantly according to first author category (medical or non-medical), study aim (diagnostic or prognostic), imaging modality (CT or MRI), and journal quartile (first or other, based on Scopus data), using the Mann–Whitney *U* test [14]. When a paper belonged to more than one category, it was counted for each category within the subanalysis. All studies published on journals whose quartile was not identified were excluded from the subanalysis. All analyses were conducted using the "stats" (v3.6.2) R package (v4.0.5) [22]. A p value < 0.05 was considered statistically significant.

Results

Literature search

In total, 1961 articles resulted from the initial search, 1245 of which were duplicates. Of the remaining 716 papers, 668 were rejected according to the selection criteria. Finally, after screening the reference lists of the eligible studies, 53 articles were included in the systematic review. The study selection flowchart is shown in Fig. 1.

Study characteristics

The characteristics of the included articles are shown in the supplementary materials. The median patient number was 76 (IQR, 50–146). Among the included studies, 36%

Table 1 Overview of radiomics quality score items and mode of the corresponding scores in the included studies

RQS checkpoint	RQS item number and name	Description and (points)	Mode
First	Item 1: Image protocol quality	Well documented protocol (+1) AND/OR publicly available protocol (+1)	1
Second	Item 2: Multiple segmentation	Testing feature robustness to segmentation variability: e.g., different physicians/algorithms/software (+1)	1
	Item 3: Phantom study	Testing feature robustness to scanner variability: e.g., different vendors/scanners (+1)	0
	Item 4: Multiple time points	Testing feature robustness to temporal variability: e.g., organ movement/expansion/shrinkage (+1)	0
Third	Item 5: Feature reduction	Either feature reduction OR adjustment for multiple testing is implemented (+3); otherwise (−3)	3
	Item 6: Multivariable analysis	Non-radiomic feature are included in/considered for model building (+1)	0
	Item 7: Biological correlates	Detecting and discussing correlation of biology and radiomic features (+1)	0
	Item 8: Cutoff analysis	Determining risk groups by either median, pre-defined cutoff or continuous risk variable (+1)	0
	Item 9: Discrimination statistics	Discrimination statistic and its statistical significance are reported (+1); a resampling technique is also applied (+1)	2
	Item 10: Calibration statistics	Calibration statistic and its statistical significance are reported (+1); a resampling technique is also applied (+1)	0
	Item 11: Prospective design	Prospective validation of a radiomics signature in an appropriate trial (+7)	0
	Item 12: Validation	Validation is missing (−5) OR internal validation (+2) OR external validation on single dataset from one institute (+3) OR external validation on two datasets from two distinct institutes (+4) OR validation of a previously published signature (+4) validation is based on three or more datasets from distinct institutes (+5)	−5
	Item 13: Comparison to "gold standard"	Evaluating model's agreement with/superiority to the current "gold standard" (+2)	0
	Item 14: Potential clinical application	Discussing model applicability in a clinical setting (+2)	2
	Item 15: Cost-effectiveness analysis	Performing a cost-effectiveness of the clinical application (+1)	0
	Item 16: Open science and data	Open-source scans (+1) AND/OR open-source segmentations (+1) AND/OR open-source code (+1) AND/OR open-source representative features and segmentations (+1)	0

RQS radiomics quality score [14]

(19/53) were published in 2020, 26% (14/53) in 2019, 19% (10/53) in 2018, 7% (4/57) in 2017, 6% (3/53) in 2021, and 2% (respectively 1/53 per year) in 2010, 2012, and 2015 (Fig. 2). In most of the studies (79%) the first author was a medical doctor. In 66% of the papers, radiomics analysis was performed as a diagnostic biomarker, in 32% as a prognostic biomarker, whereas in the remaining 2% radiomics analysis was adopted for both intended uses. MRI was the most used imaging technique (66%), whereas CT was adopted in 32% of the investigations; the remaining study (2%) used both imaging techniques.

Study evaluation

Results are summarized in Table 2. Overall, the 53 included studies reached a median total RQS of 7 (IQR, 4–12), corresponding to a percentage of 19.4% (IQR, 11.1–33.3%) (Fig. 3) [14]. Figure 4 shows the total RQS distribution across the years, with an increasing trend overall [14]. In regard to the first RQS checkpoint (item 1), 89% of the included articles provided comprehensive information on the adopted imaging protocol, with only one study (2%) obtaining the maximum number of points (2) [14]. In the second RQS checkpoint (items from 2 to 4), 55% of the studies tested feature robustness to segmentation variability, none of them evaluating inter-vendor and/or inter-scanner sources of variability, whereas only one study (2%) assessed temporal variability [14]. For items included in the third RQS checkpoint (from 5 to 16), appropriate feature reduction techniques were adopted in 75% of the included studies, and 23% of the investigations combined radiomics and non-radiomics features in multivariable analyses [14]. Correlation between biology and radiomics was discussed in 28% of the papers and 30% provided a cutoff analysis. Discrimination statistics results were usually provided (92%), whereas none of the studies employed calibration statistics, and only 4% of the studies relied on prospectively acquired data. Moreover, internal validation was performed in 45% of the studies, whereas the remaining articles did not include a formal validation of their results. Less than half of the

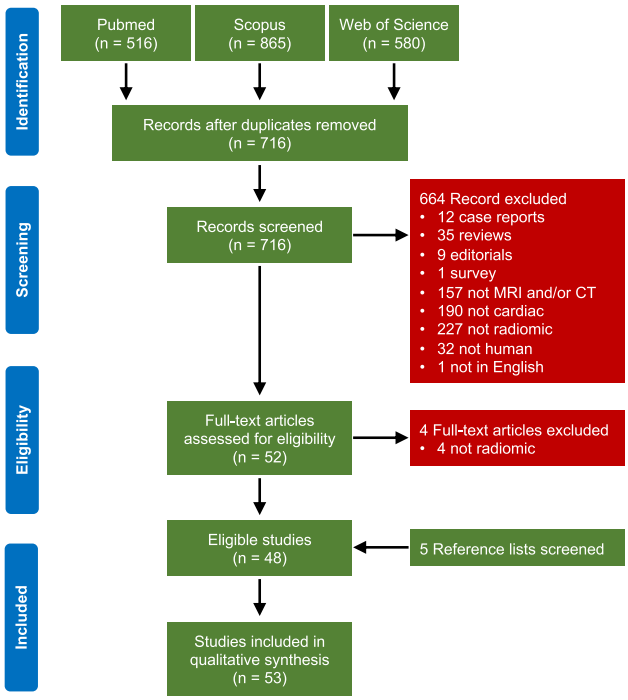

Fig. 1 Literature search and study selection process flowchart

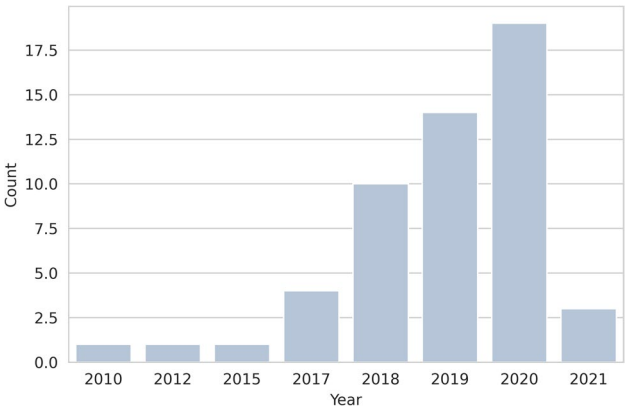

Fig. 2 Bar plot depicting the number of MRI and CT radiomics studies focused on cardiac imaging published over the years

papers (47%) proposed a direct comparison between radiomics and the gold standard and most of them (94%) addressed clinical utility. Finally, none of the studies performed a cost-effectiveness analysis, and only one article (2%) made their code and data publicly available.

Subgroup analysis

The results of the subgroup analysis according to the first author category, study aim, imaging modality, and journal quartile are shown in Table 3 and Fig. 5. In particular, in studies where the first author was a medical doctor, the total RQS was significantly higher ($p = 0.04$) [14]. Similarly, studies published on first quartile journals received significantly higher scores than those published on second or third quartiles journals ($p = 0.01$). Moreover, studies employing MRI tended to have slightly higher total RQS than those using CT (median 7.5 vs. 6.5), but this trend was not statistically significant ($p = 0.5$). Similarly, no statistically significant differences ($p = 0.4$) were found between papers according to the study aim [14].

Discussion

Several studies have shown promising results using radiomics as a diagnostic or prognostic biomarker for multiple purposes in cardiac imaging [23, 24]. However, applications of these techniques remain essentially confined to academic research [25–27]. In our review, we have found that the overall methodological quality of radiomics studies in cardiac MRI and CT is still low, with a median RQS total score of 7, corresponding to 19.4% of the ideal rating [14]. Our results are in line with previously published studies in oncologic field [18, 21, 28, 29], suggesting that these issues do not affect cardiac imaging specifically but are common across radiomics research. In particular, Zhong et al. [29] reported in their systematic review of radiomics studies in osteosarcoma a RQS [14] total score of 6.92 (20.4%), Stanzione et al. [18] of 7.93 (23%) for prostate MRI, and Ugga et al. [21] of 6.96 (19%) for meningioma. On a positive note, the total RQS percentage tends to increase across years until 2020, reflecting a continuous improvement of methodological quality for these studies in the field of cardiac imaging [14]. While this trend appears to slow down in 2021, it should be taken into account that our systematic review included investigations published up to the 7th of February of 2021, determining a limited sample for this year.

The current systematic review highlighted several characteristics bringing together the included investigations that should be implemented in future cardiac imaging research. Regarding the first item of RQS, the lack of a detailed description of the adopted protocol represents a major issue, limiting the reproducibility and consequently validation of the reported findings [14]. However, in our systematic review, most studies provided comprehensive details of the imaging acquisition protocol. The included studies proved to be of highly insufficient quality in testing feature robustness to scanner or temporal variability, also due to the predominant retrospective nature of the investigations. Indeed, in order to maximize the effectiveness of radiomics, quantitative features should be reproducible and robust versus minor variations in the image acquisition parameters as well as to organ motion or expansion

Table 2 Radiomics quality scores for all included studies

Author (year)	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	RQS (total)	RQS (%)
Alis (2019)	0	1	0	0	3	0	1	1	2	0	0	-5	2	2	0	0	7	19.4
Amano (2018)	1	0	0	0	-3	0	0	1	1	0	0	-5	0	2	0	0	-3	0
Amano (2020)	1	0	0	0	3	1	1	1	0	0	0	-5	0	2	0	0	4	11.1
Baessler (2017)	1	1	0	0	3	0	0	0	2	0	0	-5	2	2	0	0	6	16.7
Baessler (2018)	1	1	0	0	3	0	1	1	2	0	0	-5	2	2	0	0	8	22.2
Baessler (2018)	1	1	0	0	3	0	1	0	2	0	0	-5	2	2	0	0	7	19.4
Baessler (2019)	1	1	0	0	3	0	1	0	2	0	0	-5	2	2	0	0	7	19.4
Cetin (2019)	1	0	0	0	3	0	0	0	1	0	0	-5	2	2	0	1	5	14
Cetin (2019)	1	0	0	0	3	0	0	0	1	0	0	2	0	2	0	0	9	25
Cetin (2020)	2	0	0	0	3	0	0	0	1	0	0	2	2	2	0	1	13	36.1
Chen (2020)	1	1	0	0	3	1	0	1	1	0	7	-5	0	2	0	0	12	33.3
Cheng (2018)	1	1	0	0	3	1	0	1	1	0	0	-5	2	2	0	0	7	19.4
Chun (2020)	1	1	0	0	3	0	1	0	1	0	0	2	2	2	0	0	13	36.1
Ebrahimian (2021)	1	0	0	0	3	0	0	0	1	0	0	-5	2	2	0	0	4	11.1
Eftestol (2012)	0	0	0	0	-3	0	1	0	2	0	0	-5	0	2	0	0	-3	0
El-Rewaidy (2020)	1	1	0	0	3	0	1	0	2	0	0	2	0	2	0	0	12	33.3
Engan (2010)	0	0	0	0	-3	0	0	0	0	0	0	-5	0	0	0	0	-8	0
Eslami (2020)	1	1	0	0	3	1	0	1	1	0	0	2	2	2	0	0	14	38.9
Esposito (2018)	1	0	0	0	3	0	1	1	1	0	0	-5	0	2	0	0	4	11.1
Gibbs (2018)	0	0	0	0	-3	1	0	1	1	0	0	-5	2	2	0	0	-1	0
Gould (2019)	1	1	0	0	-3	1	0	1	1	0	0	-5	0	2	0	0	-1	0
Gould (2020)	1	0	0	0	-3	1	0	1	0	0	0	-5	0	2	0	0	-3	0
Hinzpeter (2017)	1	1	0	0	3	0	0	1	2	0	0	-5	0	2	0	0	5	13.9
Hu (2020)	1	1	0	0	3	1	0	0	1	0	0	2	2	2	0	0	13	36.1
Kang (2020)	1	1	0	0	3	0	0	0	2	0	0	2	0	2	0	0	11	30.6
Kay (2020)	1	0	0	0	3	0	0	0	2	0	0	2	0	2	0	0	10	27.8
Kolossvàry (2017)	1	0	0	0	-3	1	0	0	2	0	0	2	2	2	0	0	7	19
Kolossvàry (2019)	1	0	0	0	3	0	0	0	2	0	0	2	2	2	0	0	12	33.3
Kolosssvàry (2021)	1	1	0	0	-3	0	0	0	0	0	0	-5	0	2	0	0	-4	0
Kotu (2015)	1	0	0	0	3	0	0	0	2	0	0	-5	0	0	0	0	1	2. 8
Kyungsung (2019)	1	1	0	0	3	0	0	0	2	0	0	2	2	2	0	0	13	36. 1
Larroza (2017)	1	0	0	0	3	0	1	0	2	0	0	-5	0	2	0	0	4	11.1
Larroza (2018)	1	1	0	0	3	0	0	0	2	0	0	2	0	2	0	0	11	30. 6
Lin (2020)	1	0	0	0	3	1	0	0	2	0	7	2	0	2	0	0	18	50
Mannil (2018)	1	1	0	0	3	0	0	0	1	0	0	2	2	2	0	0	12	33.3
Mannil (2019)	1	1	0	0	3	0	0	0	1	0	0	2	2	2	0	0	12	33.3
Mannil (2020)	0	1	0	0	3	0	0	0	2	0	0	2	0	2	0	0	10	27.7

Table 2 (continued)

Author (year)	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	RQS (total)	RQS (%)
Muthulakshmi (2020)	1	0	0	0	3	0	1	0	2	0	0	-5	0	2	0	1	5	14
Neisius (2019)	1	1	0	0	3	0	1	0	1	0	0	2	2	2	0	0	13	36.1
Neisius (2019)	1	1	0	0	3	0	0	0	2	0	0	2	0	2	0	0	11	30.6
Oikonomou (2019)	0	1	0	0	3	0	1	1	2	0	0	2	0	2	0	0	12	33.3
Quanmei (2020)	1	1	0	0	3	0	0	0	2	0	0	2	2	2	0	0	13	36.1
Quanmei (2020)	1	1	0	0	3	1	0	0	1	0	0	2	2	2	0	0	13	36.1
Schofield (2019)	1	0	0	1	-3	0	0	0	1	0	0	-5	0	2	0	0	-3	0
Shao (2018)	1	0	0	0	-3	0	0	0	1	0	0	2	0	2	0	0	3	8.3
Shi (2021)	1	1	0	0	3	0	0	0	2	0	0	-5	2	2	0	0	6	16.7
Son (2020)	1	1	0	0	3	0	0	1	2	0	0	-5	2	2	0	0	7	19.4
Tsuneta (2020)	1	1	0	0	-3	0	0	0	1	0	0	-5	2	2	0	0	-1	0
Van Hamersvelt (2019)	1	0	0	0	3	0	1	0	2	0	0	-5	2	2	0	0	6	16.7
Van-Truong (2020)	1	0	0	0	-3	1	0	1	1	0	0	-5	0	2	0	0	-2	0
Wang (2020)	1	0	0	0	3	0	1	0	1	0	0	2	0	2	0	0	10	27.8
Wu (2018)	1	1	0	0	-3	0	0	1	1	0	0	-5	0	0	0	0	-4	0
Zhang (2019)	1	0	0	0	3	0	0	0	2	0	0	2	0	2	0	2	12	33

The total score ranges from −8 to 36, while the percentage is calculated on a 0-36 scale. RQS indicates radiomics quality score [14]

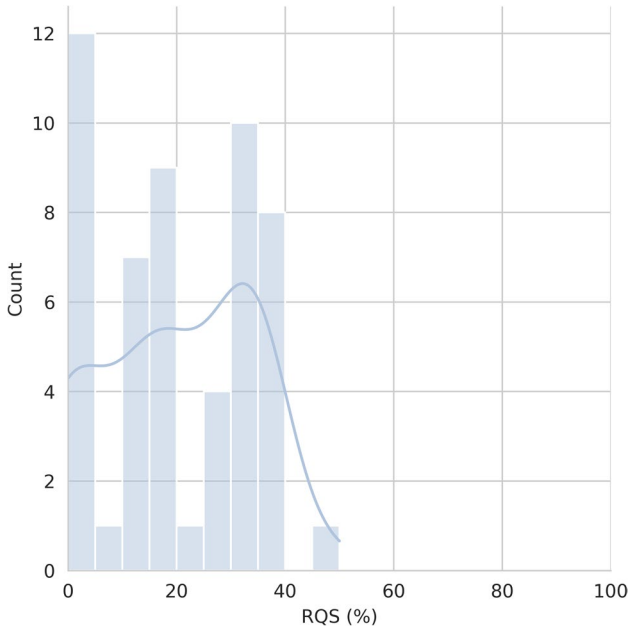

Fig. 3 Histogram of radiomics quality score in the included papers, with corresponding kernel density estimation

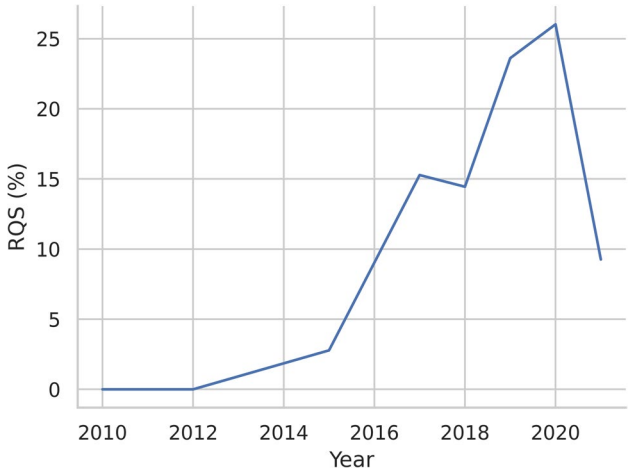

Fig. 4 Line plot of radiomics quality score in the reviewed papers over the years

[30]. However, if for single-center studies it could be difficult to evaluate inter-scanner and inter-vendor variability, other sources of heterogeneity should be explored at least, for example, with test–retest data. Considering the high dimensional nature of radiomics features that can be extracted from medical images, it is critical to reduce their number eliminating those lacking in robustness, especially for studies recruiting a small number of patients [14]. Of note, 75% of the included investigations adopted appropriate feature reduction techniques in order to avoid the risk of overfitting.

Only 28% of the studies discussed the biological correlation between biology and radiomics. However, it should be taken into account that the concept of biological correlate does not clearly fit the setting of cardiac imaging contrary to oncological fields [29, 31]. Noteworthy, only 4% of the studies relied on prospectively acquired data. As a matter of fact, adopting prospective studies, where hypotheses are established in advance, helps to reduce the risk of reporting bias [32]. While the lack of prospective studies can be justified by the relative novelty of radiomics, after almost a decade and numerous studies published on various topics, the time has probably come for appropriately designed prospective trials. Either internal or preferably external validation techniques must be adopted to evaluate model performance. Although the need for validation for imaging biomarkers has been widely claimed [33, 34], it is quite concerning that more than half of the included studies did not include a formal validation of their results.

In agreement with previously published papers [18, 21, 29], none of the included studies performed a cost-effectiveness analysis. Although sharing datasets and/or codes is encouraged [35], in our systematic review, only 8% of studies proved to be "open-minded." Publicly available datasets such as Cancer Imaging Archive [36] and the RIDER dataset [37] may indeed allow verification and reproducibility of the reported findings.

Subgroup analysis demonstrated that in papers where the first author was a medical doctor, RQS total score was significantly higher [14]. We could speculate that medical categories were more interested in discussing model applicability in a clinical setting than the not medical ones. Of note, papers published on first quartile journals received significantly higher scores than those published on second or third quartile ones. It could be argued that high-impact journals were more demanding in terms of methodological quality, especially regarding formal validations of radiomics results.

This study presents some limitations that should be acknowledged. First, a number of studies included in this review were published before the introduction of the RQS [14]. Second, radiomics is a continuously evolving imaging biomarker, and maybe the proposed RQS could be too "hypothetical," also paying the price in terms of adaptability to different study aims and scope [14]. Third, the evaluation of the methodological quality of the investigations was performed by two readers in consensus, thus not exploring inter-reader variability. However, all raters have previous experience in RQS assessment with good to moderate inter-reader reproducibility [14, 21].

In conclusion, studies focusing on radiomics-based cardiac imaging showed an overall insufficient methodological quality. A more standardized methodology in the radiomics workflow is needed, especially in terms of study

Table 3 Subgroup analysis according to first author category, study aim, imaging modality, and journal quartile

Group	Studies (*n*)	RQS total	RQS percentage	*p* value
First author category				0.04
Medical	42	7.5 (4.2–12)	20.8 (11.8–33.3)	
Non-medical	11	4 (1.5–7)	11.1 (0–19.4)	
Study aim				0.4
Diagnostic	36	7 (4.7–12)	19.4 (13.2–33.3)	
Prognostic	18	6.5 (–1.7–12)	18 (0–33.3)	
Imaging modality				0.5
MRI	36	7.5 (3.7–12)	20.8 (10.4–33.3)	
CT	18	6.5 (4–11.5)	18 (11.1–31.9)	
Journal quartile				0.01
First	35	10 (5.5–12)	27.8 (15.3–33.3)	
Others	15	4 (2–7)	11.1 (0–19.4)	

Values are expressed as number or median (interquartile range)

RQS radiomics quality score [14]

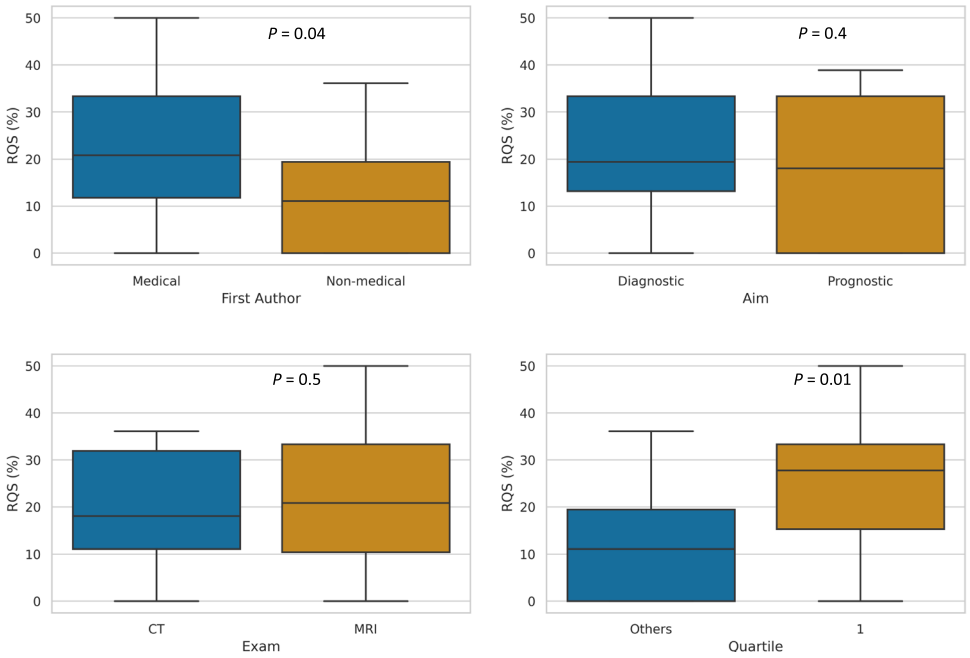

Fig. 5 Box and whisker plots showing radiomics quality score (%) distribution in relation to the subanalyses performed in the study

design, validation, and open science, in order to translate the results to clinical applications. RQS could be used either as a useful tool to assess the methodological scientific quality of the investigation either as a self-checklist before study design, thus helping researchers crossing the translational line between an exploratory investigation method and a standardized added value to precision medicine workflows [14].

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Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors (RC) has significant statistical expertise.

Informed consent Written informed consent was not required for this study because of the nature of our study (systematic review).

Ethical approval Institutional Review Board approval was not required because of the nature of our study (systematic review).

Methodology
- systematic review
- performed at one institution

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