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RESEARCH

Assessing the role of CT imaging in identifying candidates for neoadjuvant chemotherapy in right colon cancer: a critical analysis

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Abstract

Background and purpose Standard treatment for localized right colon cancer is radical surgery, followed by adjuvant chemotherapy for stage III or intermediate MSS and high-risk stage II tumours. Recent studies suggest a benefit from neoadjuvant chemotherapy (NAC), particularly for T4b and/or N + tumours. Patient selection for NAC relies on CT-based clinical staging, but the accuracy of CT in detecting high-risk features is variable, raising concerns about potential overtreatment. The study aims to demonstrate the accuracy of CT staging of the right colon with the purpose of indicating neoadjuvant CT.

Methods Patients undergoing curative right hemicolectomy between 2013 and 2023 at two Portuguese institutions were included. All had preoperative CT; those receiving NAC were excluded. Sensitivity, specificity, positive predictive value, and negative predictive value of CT in identifying T4b and N + tumours were calculated by comparing clinical (cTNM) and pathological (pTNM) staging.

Results Among 165 patients (48% male, mean age 70.5 years), CT showed low sensitivity (26%) but high specificity (91%) for pT4b tumours, with a tendency toward understaging. For nodal disease, sensitivity was 87% and specificity 41%. Only 57% of cT4b and/or cN + cases confirmed at least one unfavorable pathological factor, implying potential overtreatment in 43% of patients if NAC were applied solely based on CT findings.

Conclusion CT remains the standard for clinical staging but demonstrates limited accuracy in identifying high-risk right colon cancers. NAC decisions should integrate additional criteria beyond CT findings to avoid overtreatment.

Keywords Right Colon Cancer · Computed Tomography · Diagnostic Accuracy · Neoadjuvant Chemotherapy · Right Hemicolectomy

Introduction

According to current European Society for Medical Oncology (ESMO) guidelines, the standard treatment for localized colon cancer consists of radical surgical resection, followed by adjuvant chemotherapy in stage III disease or high-risk stage II disease. However, the most recent National Comprehensive Cancer Network (NCCN) guidelines also recommend neoadjuvant chemotherapy (NAC) in patients with adverse prognostic factors, namely T4b stage and/or locoregional nodal involvement [1, 2].

Given that the major prognostic determinant in localized colon cancer is the risk of distant metastasis [3], early systemic control through NAC could improve long-term outcomes. This is particularly relevant in locally advanced, but resectable tumours, which show recurrence rates of 20–30%. When treated with up-front surgery, these tumours present a

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3-year DFS of only 53%, compared with 87% in lower-risk tumours [4–9].

The phase III FOxTROT (Fluoropyrimidine Oxaliplatin and Targeted Receptor Pre-Operative Therapy) trial provided robust evidence supporting NAC in locally advanced but resectable (T4 and high risk T3, Nx and M0) colon cancer [10]. Patients randomized to preoperative oxaliplatin-5FU followed by surgery achieved a 28% reduction in 2-year recurrence, higher R0 resection rates (94% vs. 89%), and significant T and N downstaging compared with those undergoing upfront surgery [4, 5, 10]. Consequently, NCCN guidelines now endorse NAC with CAPOX or FOLFOX in cT4b Nx or cTx N + cases, followed by curative surgery and adjuvant chemotherapy.

There is significant biological and clinical heterogeneity within T4 disease. T4a tumours, are characterized by invasion of the visceral peritoneum and are associated with a considerably higher 5-year survival rate (approximately 80%) compared with T4b tumours, which directly invade or adhere to adjacent organs or structures [2]. In right-sided colon cancers, given that the posterior wall is retroperitoneal and lacks peritoneal coverage, tumours arising from the posterior wall of the right colon with invasion of the retroperitoneal fascia – a feature associated with a high incidence of synchronous and metachronous distant metastasis—are classified as T4b [2, 11]. Furthermore, since bowel wall invasion is frequently misclassified on preoperative CT, high-risk T3 tumours (defined by extramural invasion ≥ 5 mm beyond the muscularis propria) with suspected retroperitonal breach may be managed as biologically similar to T4b disease in contemporary NAC algorithms [2, 12, 13].

Accurate preoperative staging is therefore essential for identifying suitable candidates for NAC. However, FOxTROT also revealed substantial limitations of computed tomography (CT)-based staging: only 47% of pT4 tumours were classified as cT4, and 50% of cT4 cases were actually pT3. Similarly, 44% of those defined as cN + at CT imaging tumours proved pathologically node-negative [4]. These findings, supported by other studies, underscore CT's variable sensitivity and specificity in T and N assessment [14]. Overstaging may lead to unnecessary chemotherapy, with risks of toxicity, surgical delay, and perioperative morbidity [4, 5, 8, 15].

Despite these concerns, previous evaluations of CT accuracy have rarely differentiated between right- and left-sided colon cancers, which differ markedly in epidemiology, molecular profile, metastatic patterns, and outcomes [16–22].

Against this background, the present study aims to evaluate the diagnostic performance of CT in staging locally advanced right-sided colon cancers and to estimate the risk of overtreatment and undertreatment if NAC were to be applied based on CT findings.

Methods

A national, multicentre, retrospective study was conducted using prospectively maintained databases from two Portuguese institutions, *Champalimaud Clinical Centre* and *Hospital de Portimão*. The study encompassed all patients who underwent elective curative-intent right hemicolectomy for right-sided colon cancer between 2013 and 2023. Eligible patients had an available preoperative CT for staging, histologically confirmed malignancy (defined by ICD-O-3), no NAC, and underwent R0 or R1 resection (with R1 defined as the presence of tumour ≤ 1 mm from the retroperitoneal margin). Patients who had received NAC, underwent R2 resection, or had incomplete clinical (cT) or pathological staging were excluded.

Collected variables included demographic data (age, sex and institution), clinical staging (tumour location and cTNM classification), and histopathological features (pTNM, tumour histology, lymph node yield, and resection type). Nodal status was dichotomized as positive or negative based on the presence of nodal metastases. Pathological staging followed the same TNM system. At both institutions, CT imaging was performed with a 1-mm slice thickness using a standard multiphasic abdominal triple-phase protocol, including non-contrast, arterial (approximately 25–35 s), and portal venous (approximately 70–80 s) phases following intravenous injection of iodinated contrast. Pathological examination at both institutions followed standard protocols, performed by gastrointestinal (GI) dedicated pathologists trained in colorectal cancer staging. In both institutions, the retroperitoneal margin was inked, and no specialized fat-clearing techniques for lymph node retrieval or routine immunohistochemistry for high-risk feature detection were used. All cases were reviewed at each institution by a team that included GI pathologists and radiologists with > 5 years of specialized experience and discussed at multidisciplinary tumour boards. Surgical interventions were also standardised and performed by dedicated colorectal surgery teams.

The primary endpoint was the diagnostic performance of CT in identifying adverse pathological features (T4b or N +). Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were calculated using pathological staging as the reference standard.

The secondary endpoints were:

1) the proportion of tumours staged as high risk (cT4b and/or cN +) that did not meet pathological criteria for neoadjuvant chemotherapy (potential overtreatment), and
2) the proportion of clinically low-risk tumours (cT1–4a N0) that were proved pathologically eligible for adjuvant chemotherapy (potential undertreatment).

All statistical analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

Results

Out of 172 patients with data on clinical and pathological staging, 2 were excluded due to R2 at pathology, 2 were excluded because they underwent NAC treatment and 3 were excluded because of histology not listed on ICD-O-3. A total of 165 patients were included, comprising 80 males (48%) and 85 females (52%), with a mean age of 70.8 years (range, 37–92 years). Overall, 81 (49%) patients presented at least one adverse pathological factor, including 7 (4%) with pT4b and 77 (47%) with pN + as seen in Fig. 1.

Only 133 patients (81%) had known clinical N status (cN0 or cN +); therefore, the comparative analysis of preoperative CT staging and histopathological findings was performed separately for T and N parameters (Table 1).

Clinical (CT) and pathological staging concordance – T stage

Clinical staging identified 58% tumours as cT3, 7% as cT4a and 6% as cT4b, whereas pathological assessment showed 62% pT3, 14% pT4a and 4% pT4b (Table 2.).

CT understaged 50 of 165 cases (30%) and overstaged 30 (18%), with an overall concordance of 52% (85/165). Among tumours staged clinically as cT4b, 56% (5/9) were found to be pT3, and 44% (4/9) pT4b. Additionally, 3 of 7 pT4b tumours (43%) were clinically understaged.

For the detection of T4b tumours, CT sensitivity was 57%, specificity was 97%, positive predictive value was 44%, negative predictive value was 98%, and accuracy was 95% (Table 3.).

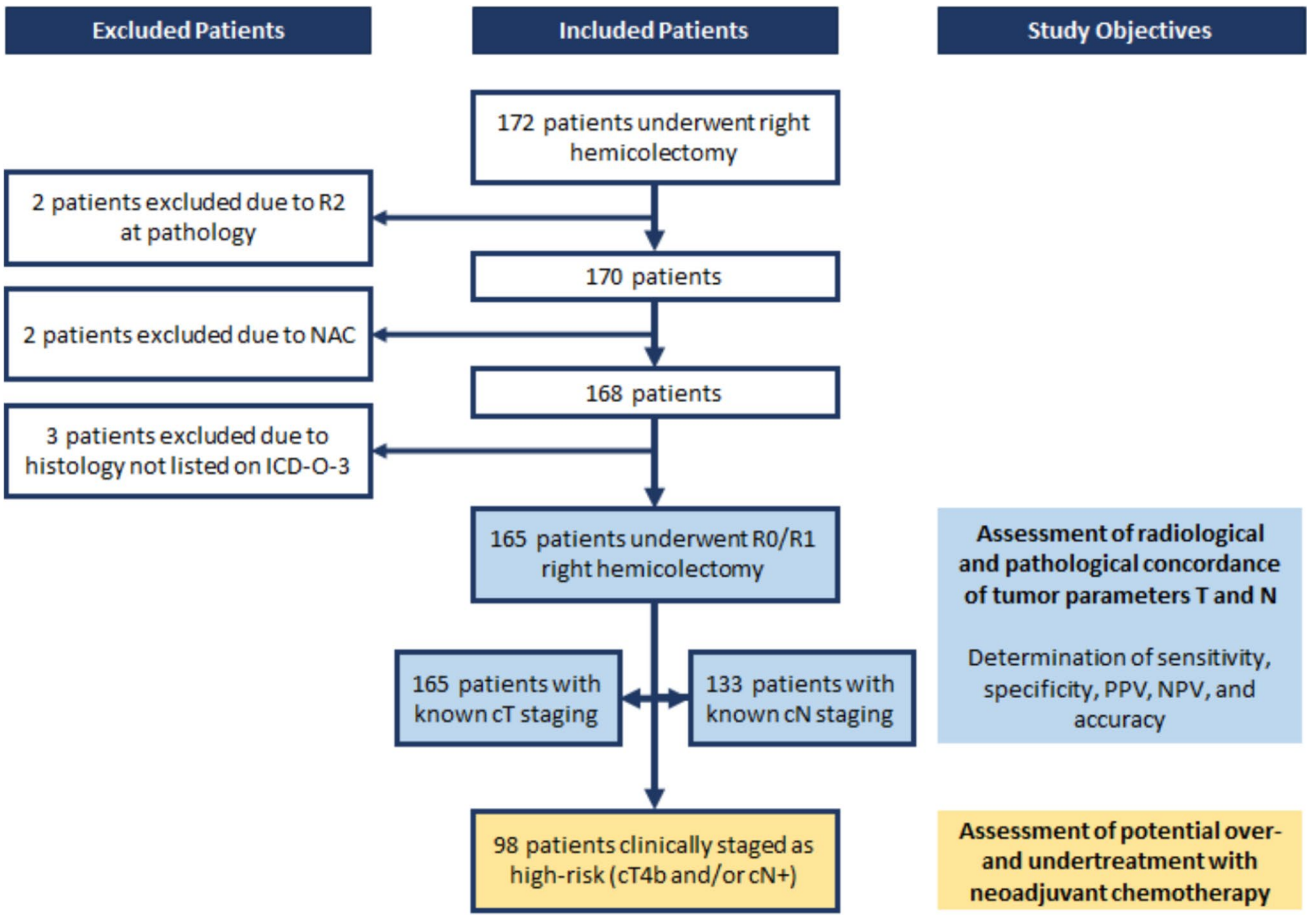

Fig. 1 Flowchart illustrating the study selection process

Table 1 Patients' demographics and clinical and histologic tumour characteristics

Sex	
Male	80 (48%)
Female	85 (52%)
Age (years)	
Mean; range	70,8; (37–92)
Institution	
C.C. Champalimaud	72 (44%)
H. Portimão	93 (56%)
Tumour Location	
Cecum	65 (39%)
Ascending Colon	52 (32%)
Hepatic Flexure	29 (18%)
Transverse Colon	19 (11%)
Lymph Nodes (LN) Excision	
No. of harvested LNs (mean; SD)	39 (22,9)
No. of positive LNs (mean; SD)	5 (4,8)
Resection Type	
R0	160 (97%)
R1	5 (3%)
T Clinical Stage (cT, n = 165)	
cT1	7 (4%)
cT2	41 (25%)
cT3	96 (58%)
cT4a	12 (7%)
cT4b	9 (6%)
N Clinical Stage (cN, n = 133)	
cN0	40 (30%)
cN +	93 (70%)
cNx	32
M Clinical Stage (cM, n = 165)	
cM0	151 (91%)
cM1	14 (9%)
T Pathological Stage (pT, n = 165)	
pT1	7 (4%)
pT2	25 (15%)
pT3	103 (63%)
pT4a	23 (14%)
pT4b	7 (4%)
N Pathological Stage (pN, n = 165 | 133)	
pN0	88 (53%) | 68 (51%)
pN +	77 (47%) | 65 (49%)
Tumour Histology (n = 165)	
Adenocarcinoma	144 (87%)
Mucinous carcinoma	17 (10%)
Signet-ring cell carcinoma	4 (3%)

Clinical (CT) and pathological staging concordance – N stage

Among the 133 patients with available cN status, CT suggested locoregional spread in 70% (93/133). Pathological staging showed 68 (51%) pN0, and 65 (49%) pN + (Table 4.).

CT overstaged nodal status in 37 of 93 cN + tumours (40%) and understaged in 9 of 40 cN0 tumours (23%), yielding an overall concordance of 65% (87/133). For detection of nodal metastases (N + disease), CT demonstrated a sensitivity of 86%, specificity of 46%, positive predictive value of 60%, negative predictive value of 78%, and overall accuracy of 65% (Table 5.).

Assessment of potential over- and undertreatment with neoadjuvant chemotherapy

Of the 165 patients, 98 (59%) were clinically staged as high-risk (9 cT4b, 93 cN +), thus meeting criteria for neoadjuvant chemotherapy (NAC). CT identified a single high-risk feature in 94 patients (96%) and both T4b and N + features in 4 patients (4%) (Table 6.).

Pathological assessment revealed discordance in 62 of 98 clinically high-risk cases (63%). Among these, 25 (40%) retained at least one adverse pathological feature (pT4b and/or pN +), thus confirming eligibility for neoadjuvant chemotherapy (NAC) despite inaccurate clinical staging. Conversely, 37 of 98 patients (38%) classified as high risk on CT had no corresponding pathological risk factors, representing potential overtreatment. One of four tumours (25%) staged as cT4bN + demonstrated no adverse pathological features.

Among the 37 tumours staged as clinically low risk (cT1–4aN0), 29 (78%) were confirmed as low-risk pathologically (Table 7.).

Eight (22%) cases harboured at least one adverse feature, cases that would have benefited from NAC but not eligible as per CT staging.

Discussion

Although endorsed by the NCCN guidelines, NAC has not yet become standard practice for locally advanced colon cancer, partly due to concerns about overtreatment when clinical staging relies solely on CT [23]. In real-life practice, CT interpretation is often challenging and subject to variability, which can potentially lead to misclassification of tumour stage and suboptimal treatment planning.

In this multicentre real-life cohort, CT showed limited performance in assessing both the depth of tumour invasion and locoregional lymph node status in right-sided colon cancer. Sensitivity for detecting pT4b tumours was reasonable (57%). In comparison, specificity was high (97%), reflecting

Table 2 Concordance between clinical and pathological T staging

		pT Staging						cT – pT Concordance		
		1	2	3	4a	4b	T	Upstaged	Unchanged	Downstaged
cT Staging	1	2	3	2	--	--	7	--	2	5
	2	3	10	21	5	2	41	3	10	28
	3	2	11	67	16	--	96	13	67	16
	4a	--	1	8	2	1	12	9	2	1
	4b	--	--	5	--	4	9	5	4	--
	T	7	25	103	23	7	165	30 (18%)	85 (52%)	50 (30%)

Table 3 Performance of CT in clinical T staging, compared with histopathology

	Se	Sp	PPV	NPV	Acc
T1	29%	97%	29%	97%	94%
T2	40%	78%	24%	88%	72%
T3	66%	53%	70%	48%	61%
T4a	9%	93%	17%	86%	81%
T4b	57%	97%	44%	98%	95%

Se sensitivity, *Sp.* Specificity, *PPV* positive predictive value, *NPV* negative predictive value, *Acc.* accuracy

a tendency toward understaging of T status. Conversely, for nodal involvement, sensitivity was high (86%) but specificity was modest (46%), resulting in frequent false positives. Overall, 38% of clinically high-risk tumours would have received unnecessary NAC, while 22% of clinically low-risk cases harboured adverse pathological features that would have justified neoadjuvant or adjuvant therapy.

These findings are broadly consistent with those of previous reports. Hernández et al. (2023) reported a sensitivity of 57% for T4 and 64% for N+, with frequent understaging (43% for T and 38% for N) and overstaging (36% for N) [14]. Nerad et al. (2016) found CT sensitivity of 90% and specificity of 69% for identifying pT3/4 disease, and 71% and 67%, respectively, for nodal status [24]. Fernández et al. (2019), in the only study focusing specifically on right-sided colon cancer, observed sensitivity and specificity of 57% and 76% for pT3/4, and 47% and 71% for pN+, respectively [7]. In contrast, earlier studies that included both right- and left-sided tumours have shown slightly higher accuracy rates, likely due to anatomical and biological differences between tumour sites [7, 14, 24]. Collectively, these data emphasise that CT tends to overestimate nodal involvement while underestimating T4b extension, particularly in right-sided tumours. These results should be interpreted in the context of a T4b classification that does not incorporate detailed characterization of retroperitoneal margin involvement. Accordingly, the accuracy of CT imaging reported in this study reflects performance in identifying T4b disease as currently defined in routine practice, rather than in predicting specific patterns of retroperitoneal margin contact, threatened margins, or true margin infiltration. Technical limitations – including reduced soft-tissue contrast, colonic peristalsis, and difficulty distinguishing tumour infiltration from inflammatory or desmoplastic reaction – may explain the reduced diagnostic performance [25–27].

Importantly, this study reflects real-world clinical conditions, where multiple radiologists interpreted CT scans according to local practice rather than being centrally reviewed. This mirrors everyday clinical decision-making, in which staging variability is inevitable. The results underline that CT-based risk stratification in localised colon cancer can be misleading, with meaningful implications for NAC selection. Overstaging may expose patients to unnecessary chemotherapy-related toxicity, surgical

Table 4 Concordance between clinical and pathological N staging

		pN Staging			CN – pN Concordance		
		0	+	T	Upstaged	Unchanged	Downstaged
cN Stag.	0	31	9	40	--	31	9
	+	37	56	93	37	56	--
	T	68	65	133	37 (28%)	87 (65%)	9 (7%)

Table 5 Performance of CT in clinical N staging, compared with histopathology

	Se	Sp	PPV	NPV	Acc
N	86%	46%	60%	78%	65%

Se. sensitivity, *Sp.* Specificity, *PPV* positive predictive value, *NPV* negative predictive value, *Acc.* accuracy

delay, and impaired fitness for resection, while understaging may result in missed opportunities for early systemic control of micrometastatic disease.

Alternative imaging modalities, including MRI, CT colonography, and PET, have been investigated to improve locoregional staging. MRI provides superior soft-tissue contrast and can better delineate T4 disease; however, its performance in nodal staging remains comparable to that of CT [7, 14, 24, 28]. CT colonography offers limited additional benefit and requires prior bowel preparation [29, 30], while PET lacks adequate spatial resolution for T and N assessment [29]. Therefore, CT remains the most practical modality for preoperative staging, though its diagnostic limitations must be acknowledged when considering NAC eligibility.

Modern imaging technologies, including three-dimensional (3D) reconstruction and artificial intelligence (AI)-based segmentation, can complement conventional CT and improve clinical staging and surgical planning for right-sided colon cancers. By enabling more precise characterization of tumour morphology, depth of infiltration, margin status, and spatial relationships with adjacent structures—including vasculature, fascia, and mesenteric planes—these tools enhance preoperative staging accuracy and risk stratification. This may optimize patient selection for neoadjuvant chemotherapy and support individualized surgical strategies, potentially reducing treatment-related complications and improving prognosis. Nevertheless, standardised protocols and prospective validation are required to ensure reproducibility and integration into routine clinical practice [31, 32].

This study comes with some limitations. Its retrospective design and modest sample size may limit generalizability. Incomplete clinical records restricted the evaluation of postoperative treatments and long-term outcomes, and a proportion of patients lacked complete nodal staging, limiting combined T and N analyses. Moreover, radiological data did not include parameters such as the presence of extramural vascular invasion (EMVI) and the presence of tumour deposits, which are integrated into the CT-TDV system recently proposed [33]. Eligibility for neoadjuvant chemotherapy in our analyses was based solely on T4b and N + status, without including high-risk T3 tumours, which may have underestimated the potential clinical impact of CT-based staging in identifying all high-risk patients. In addition, the number of cT4b cases was 9 and of pT4b cases of 7, the size of this category of patients limits the generalizability of our results. In this real-world cohort, detailed radiological descriptors of the retroperitoneal margin, as contact with the retroperitoneal fascia or the presence of threatened margins, were not systematically reported and therefore could not be analysed as independent variables. Consequently, cases were classified according to the binary pT4b definition. This represents a limitation of the study when interpreting the ability of

Table 6 Comparison of clinical and pathological staging of tumours preoperatively defined as eligible for neoadjuvant chemotherapy according to NCCN/FOxTROT study criteria

	Clinical Staging	Histological Confirmation[a]	NAC Criteria Maintained[b]	Overtreatment
T4b Nx/0	5	2 (40%)	4 (80%)	1 (20%)
T1,2,3,4a N+	89	33 (37%)	54 (61%)	35 (39%)
T4b N+	4	1 (25%)	3 (75%)	1 (25%)
	98	**36 (37%)**	**61 (62%)**	**37 (38%)**

A – Cases with histopathological confirmation of preoperative staging defined by CT. b – Cases in which, regardless of histopathological confirmation of preoperative staging, criteria for neoadjuvant chemotherapy eligibility are maintained

Table 7 Assessment of eligibility for adjuvant chemotherapy and, consequently, for neoadjuvant chemotherapy in tumours clinically considered low risk for metastasis

	Pathological Staging			Undertreatment
Clin. Stag.	T1,2,3,4a N0	T1,2,3,4a N+	T	
T1,2,3,4a N0	29	8	37	8 (22%)

preoperative CT imaging to predict retroperitoneal margin risk. At the same time, this approach reflects common daily reporting practices, which may themselves contribute to the challenges of accurately integrating margin-specific risk stratification into preoperative decision-making.

CT remains the gold-standard imaging modality for initial staging; however, its variable performance in detecting high-risk features leads to an unavoidable risk of both overstaging and undertreatment. Decisions regarding NAC should therefore be made cautiously and always within a multidisciplinary context. Future studies should assess the integration of refined radiological parameters, such as EMVI, tumour deposits, retroperitoneal margins threatening or involvement, and explore the potential of combined imaging approaches – particularly CT and MRI – and emerging imaging technologies, as 3D reconstructions and AI-based segmentation, to enhance the precision of preoperative staging and optimise patient selection for neoadjuvant strategies.

Author contributions J.L.L., M.C., J.A., L.M.F., E.A. conceived the work. J.L.L., A.S.S.S., B.M. collected and analysed the data. All authors reviewed the data and defined the structure of the manuscript. J.L.L. performed the analysis and prepared tables and figures. J.L.L., E.P.T., M.C. and J.A. wrote the manuscript. and C.D. wrote the main manuscript text and E.F. prepared Figure and tables. 1-. J.A., L.M.F., M.C. and A.P. supervised the study and the manuscript preparation. All authors reviewed the manuscript.

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Data availability The dataset is not publicly available but may be requested to the corresponding author upon reasonable request.

Declarations

Ethics approval This multicentre retrospective study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the institutional review boards of all participating centres. Given the retrospective nature of the study and the use of anonymized data, the requirement for informed consent was waived by the respective ethics committees.

Competing interests Authors declare no competing interests for this work.

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