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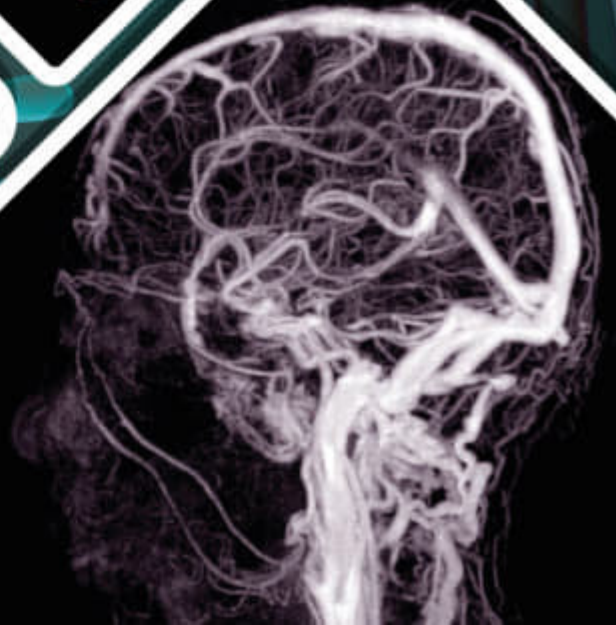
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Haemodynamic effects of carotid artery stenting on cerebral perfusion: a CT perfusion study

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ABSTRACT

Aims: To evaluate quantitative cerebral haemodynamic alterations using computed tomography perfusion (CTP) imaging before and after carotid artery stenting (CAS) in patients with severe internal carotid artery (ICA) stenosis.

Methods: This retrospective study included 34 symptomatic patients (23 males, 11 females; mean age 65±9 years) with unilateral high-grade ICA stenosis (≥70% according to NASCET criteria) confirmed by digital subtraction angiography. Baseline cerebral CTP examinations were performed using a 64-detector CT scanner. Symmetrical cortical regions of interest were analyzed to obtain relative cerebral blood volume (rCBV), relative cerebral blood flow (rCBF), and relative mean transit time (rMTT) indices, using the contralateral hemisphere as the 100% reference. Early follow-up CTP examinations were performed 24-48 hours after successful CAS in 14 patients with marked baseline perfusion abnormalities.

Results: Pre-treatment analysis demonstrated significant interhemispheric haemodynamic asymmetry. The stenotic hemisphere showed significantly elevated rCBV and prolonged rMTT values (106%±8%; p=0.0001 for both). Relative cortical perfusion analysis also revealed increased rCBF indices (115%±17%; p=0.0002). Following CAS, significant haemodynamic normalization was observed. Postprocedural rCBV and rCBF values decreased toward physiological ranges (108%±8%, p=0.0016; 112%±12%, p=0.0073, respectively), while rMTT shortened to near-normal levels (98%±4%; p=0.0001). No significant correlation was identified between stenosis severity and CTP-derived haemodynamic indices (p>0.05).

Conclusion: Severe carotid artery stenosis was associated with significant cerebral perfusion abnormalities and interhemispheric haemodynamic asymmetry. Among patients undergoing follow-up evaluation, significant normalization of CTP-derived perfusion parameters was observed after CAS. These findings suggest that quantitative CTP may provide useful information for assessing haemodynamic impairment and monitoring early post-procedural perfusion changes.

Keywords: Carotid stenosis, computed tomography, perfusion imaging, hemodynamics

INTRODUCTION

Carotid artery stenosis is a leading cause of ischaemic cerebrovascular disease and remains an important source of morbidity and mortality worldwide.^{1,2} Atherosclerotic narrowing of the internal carotid artery (ICA) may result in decreased cerebral perfusion pressure, impaired cerebrovascular reserve capacity, and subsequent cerebral ischaemia.² Severe carotid artery stenosis has been strongly associated with transient ischaemic attacks, ischaemic stroke, cognitive decline, and chronic cerebral hypoperfusion.³ As ischaemic stroke continues to be among the most common causes of long-term disability and death, early diagnosis and timely treatment of carotid artery disease are of major clinical importance.²

The degree of carotid stenosis alone may not fully reflect the haemodynamic impact of the disease on cerebral circulation. In patients with significant stenosis, compensatory autoregulatory mechanisms initially preserve cerebral blood flow (CBF) through vasodilatation and collateral circulation.⁴ However, progressive stenosis may eventually exceed the compensatory capacity of cerebral vessels, leading to deterioration of cerebral perfusion and increased risk of irreversible neuronal injury. Therefore, direct assessment of cerebral haemodynamics provides valuable information beyond anatomical evaluation alone.^{2,4}

Conventional imaging methods, including Doppler ultrasonography, computed tomography angiography,



magnetic resonance angiography, and digital subtraction angiography, primarily provide anatomical data regarding the severity of vascular narrowing.²⁻⁵ However, these techniques remain limited in evaluating the functional and microcirculatory consequences of stenosis.⁶ In contrast, computed tomography perfusion (CTP) imaging allows for a rapid, non-invasive, and quantitative assessment of regional cerebral haemodynamics by measuring parameters such as CBF, cerebral blood volume (CBV), and mean transit time (MTT).⁷⁻⁹ Although previous literature notes that carotid artery stenting (CAS) can alleviate perfusion deficits, quantitative data on post-interventional haemodynamic tracking in routine clinical practice remain limited.¹⁰ Therefore, the aim of this study was to quantitatively evaluate dynamic cerebral perfusion changes before and after CAS using CTP in patients with high-grade ICA stenosis.

METHODS

Ethics

This study was conducted with the approval of the Medical Ethics Committee of the Faculty of Medicine at Gaziantep University (Date: 26.04.2012, Decision No: 199). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. This manuscript was derived from the medical specialty thesis of Ayhan Duman conducted at Gaziantep University Faculty of Medicine, Department of Radiology, Gaziantep, Türkiye.

Study Design and Patient Population

This retrospective study included 34 patients with unilateral ICA stenosis who underwent carotid angiography and CAS at our institution. The degree of stenosis was determined according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria, and only patients with stenosis of 70% or greater were included.

All 34 patients included in this retrospective cohort were symptomatic, presenting with a documented clinical history of ipsilateral hemispheric transient ischaemic attack (TIA) or minor ischaemic stroke within the 6 months prior to deployment. CAS indications were strictly based on multidisciplinary consensus confirming high-grade narrowing associated with neurological symptoms.

All patients underwent cerebral CTP imaging before CAS to evaluate cerebral haemodynamics associated with severe carotid artery stenosis. Patients with intracranial haemorrhage, intracranial mass lesions, previous major territorial cerebral infarction, severe motion artefacts on perfusion imaging, or incomplete clinical and radiological data were excluded.

To minimise the influence of acute ischaemic changes on cerebral perfusion measurements, diffusion-weighted magnetic resonance imaging (MRI) was performed before perfusion CT imaging in all patients. Clinical records and imaging findings were retrospectively reviewed using the institutional picture archiving and communication system (PACS) and hospital database.

CT Perfusion Imaging Protocol

Cerebral CTP examinations were performed utilizing a 64-detector CT scanner (General Electric Healthcare, Milwaukee, WI, USA). The contrast administration protocol consisted of a 40 ml bolus of non-ionic iodinated contrast medium (300 mg I/ml) followed by a 30 ml saline flush, delivered via an automated power injector through an antecubital vein at a strict injection rate of 4.0 ml/s. Dynamic scanning parameters were initiated with a fixed 5-second acquisition delay.

Quantitative assessment was performed using GE Perfusion 4 software. Circular and oval regions of interest (ROIs) measuring 60-100mm² were symmetrically and manually placed on axial slabs at the anatomical level of the basal ganglia, specifically targeting the cortical middle cerebral artery (MCA) territories while carefully avoiding major superficial cortical branches and the superior sagittal sinus.

A "marked perfusion abnormality" was operationally defined as an inter-hemispheric relative mean transit time (rMTT) delay >2.0 "seconds" or an asymmetry index >15% in the stenotic cortex compared to the normal side. The 14 patients who underwent follow-up imaging represented the specific subgroup meeting these severe hemodynamic stress criteria at baseline. Follow-up CTP examinations for this subgroup were systematically performed 24 to 48 hours post-procedure to assess immediate revascularization outcomes and monitor for potential hyperperfusion phases.

Perfusion parameters, including CBF, CBV, and MTT, were evaluated in all patients. Quantitative perfusion measurements from the cerebral hemisphere ipsilateral to the carotid artery stenosis were compared with those from the contralateral hemisphere.

CTP imaging was used to assess cerebral haemodynamic alterations associated with carotid artery stenosis and to evaluate perfusion changes after CAS in selected patients.

Carotid Artery Stenting Procedure

CAS procedures were performed under angiographic guidance by experienced interventional radiologists. Endovascular treatment was used to restore luminal patency in the stenotic internal carotid artery.

All interventional procedures were performed via a retrograde transfemoral artery approach under local anaesthesia. Endovascular reconstruction was carried out using self-expanding nitinol stents (Carotid WALLSTENT, Boston Scientific, Marlborough, MA, USA/Acculink, Abbott Vascular, Santa Clara, CA, USA). To minimize thromboembolic complications during the procedure, distal embolic protection devices (FilterWire EZ, Boston Scientific/Emboshield, Abbott Vascular) were universally deployed in all 34 cases before target lesion crossing and dilation.

Diagnostic angiographic examinations were performed to evaluate the degree of carotid stenosis before treatment. Following stent placement, angiographic control images were obtained to assess vascular patency and postprocedural luminal restoration.

Image Analysis

Perfusion parameters of the stenotic and contralateral hemispheres were comparatively analysed in all 34 patients. Differences between hemispheres were evaluated to determine the haemodynamic effects of severe carotid artery stenosis on cerebral circulation.

In addition, follow-up CTP imaging after CAS was performed in 14 patients with marked preprocedural perfusion abnormalities. Pre-treatment and post-treatment perfusion parameters were compared to evaluate cerebral haemodynamic improvement after revascularisation.

Changes in cerebral blood flow, cerebral blood volume, and MTT values after CAS were analysed to determine the effects of endovascular treatment on cerebral perfusion.

Statistical Analysis

Continuous perfusion parameters were expressed as mean±standard deviation (SD). Data normality was evaluated using the Shapiro-Wilk test. Inter-hemispheric differences (stenotic vs. contralateral normal) and longitudinal alterations (pre-stenting vs. post-stenting) were analyzed using the paired Student's t-test for normally distributed variables and the Wilcoxon signed-rank test for non-parametric datasets.

Bivariate correlations between the anatomical NASCET stenosis percentages and quantitative relative CTP indexes were calculated using Spearman's rank correlation coefficient (r). Statistical significance was defined as $p < 0.05$.

RESULTS

Among the 34 patients, preprocedural quantitative perfusion analysis demonstrated significant hemodynamic asymmetry between the hemisphere ipsilateral to the severe carotid artery stenosis and the contralateral unaffected hemisphere. Symmetrical ROI evaluations revealed significantly elevated relative cerebral blood volume (rCBV) indices and prolonged rMTT values ($106\% \pm 8\%$) in the stenotic hemisphere ($p = 0.0001$ for both). Relative cortical perfusion analysis also demonstrated increased rCBF indices in the stenotic hemisphere ($115\% \pm 17\%$, $p = 0.0002$) (Figure).

Among the 14 patients who underwent follow-up CT perfusion imaging after carotid artery stenting, significant improvement in cerebral perfusion parameters was observed following revascularisation. Postprocedural analyses showed

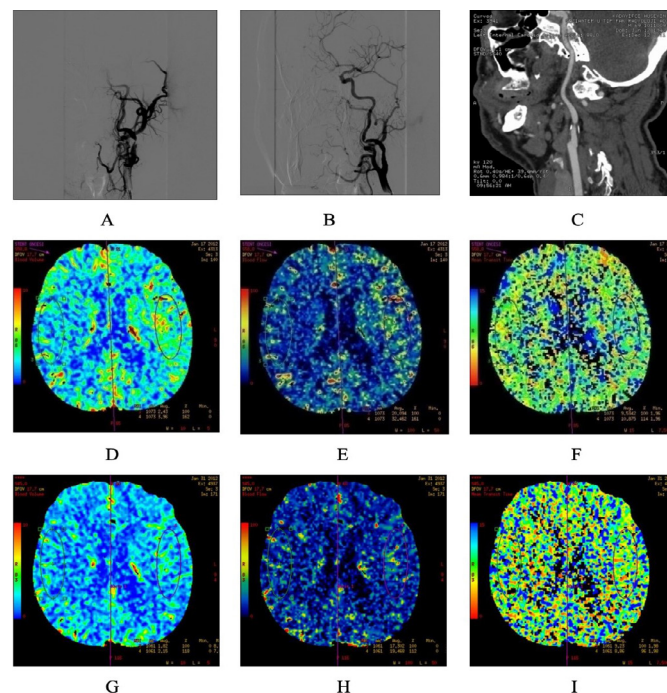


Figure. Multimodal imaging alignment and standardized perfusion tracking of a 69-year-old male patient (Case 1) presenting with a 95% symptomatic stenosis of the left internal carotid artery (ICA)

(A) Pre-stenting digital subtraction angiography (DSA) demonstrating severe luminal obstruction at the ICA origin. (B) Post-stenting DSA confirming excellent structural restoration and luminal patency. (C) Computed tomography angiography (CTA) showing the anatomical narrowing. (D-F) Pre-stenting cerebral blood volume (rCBV), cerebral blood flow (rCBF), and mean transit time (rMTT) perfusion maps. Symmetrical circular region of interest (ROI) templates are digitally overlaid on matching axial coordinates at the basal ganglia level to track microvascular asymmetry. Note the baseline delay in transit time (rMTT) coupled with compensatory cortical rCBV preservation. (G-I) Post-stenting rCBV, rCBF, and rMTT perfusion maps obtained using identical mathematical color-scale thresholds. Postprocedural panels demonstrate direct objective hemodynamic normalization, marked by a significant contraction of the over-dilated capillary beds back to physiological baselines and the prompt shortening of tissue transit time (rMTT).

normalisation of perfusion findings, with reduction of CBV and CBF values towards normal ranges and shortening of MTT.

Comparisons between pre-treatment and post-treatment perfusion measurements showed statistically significant changes after carotid artery stenting. Postprocedural reductions in CBV ($p = 0.0016$) and CBF ($p = 0.0073$), together with shortening of MTT ($p = 0.0001$), indicated improvement in cerebral haemodynamics after restoration of carotid blood flow.

Spearman's correlation analysis demonstrated no statistically significant correlation between the anatomical percentage of ICA luminal narrowing and quantitative preoperative perfusion parameters (all $p > 0.05$).

Absolute perfusion measurements and relative perfusion indices before and after CAS are summarised in Table.

Table. Cerebral perfusion parameters before and after carotid artery stenting

Parameter	Contralateral hemisphere (n=34)	Pre-CAS stenotic hemisphere (n=34)	Post-CAS stenotic hemisphere (n=14)	p ¹	p ²
CBV (ml/100 g)	2.05±0.66	2.36±0.73	1.96±0.48	0.0001	0.0016
rCBV (%)	100	116±21	107.2±10.0	0.0001	0.0016
CBF (ml/100 g/min)	18.27±4.95	20.96±6.16	17.65±3.98	0.0002	0.0073
rCBF (%)	100	115.7±21.4	111.6±13.4	0.0002	0.0073
MTT (s)	8.98±1.35	9.56±1.22	9.12±0.85	0.0001	0.0001
rMTT (%)	100	106.7±6.9	98.6±3.8	0.0001	0.0001

Data are presented as mean ± standard deviation (SD). Relative indices were calculated using the contralateral hemisphere as the reference (100%). CAS: Carotid artery stenting, CBV: Cerebral blood volume, CBF: Cerebral blood flow, Min: Minute, MTT: Mean transit time, r: Relative, p¹, stenotic vs contralateral comparison; p², pre-CAS vs post-CAS comparison

DISCUSSION

Carotid artery stenosis is a major cause of cerebral hypoperfusion and ischaemic cerebrovascular disease.² Progressive luminal narrowing in the carotid artery may lead to reduced cerebral perfusion pressure and impaired cerebrovascular reserve, increasing the risk of TIA and ischaemic stroke.^{2,3} In clinical practice, accurate evaluation of cerebral haemodynamics is important not only for determining the severity of stenosis but also for treatment planning and postprocedural follow-up.⁴

In our study, preoperative dynamic CTP maps demonstrated an intriguing cortical perfusion pattern in the hemisphere ipsilateral to the high-grade ICA stenosis. While classic severe arterial inflow restrictions typically lead to a reduction in absolute global tissue blood supply, our regional cortical ROI measurements exhibited elevated rCBF and rCBV indexes alongside significantly prolonged rMTT values. This particular phenomenological pattern can be physiologically explained by the breakdown or limits of local autoregulatory capacity.⁴ In chronic high-grade stenosis, the severe reduction in perfusion pressure induces maximal pre-capillary compensatory vasodilatation to maintain tissue viability.^{2,4}

This structural widening of the microvascular bed, which expands the regional blood pool to maintain tissue viability, mathematically biases the first-pass deconvolution software algorithms.⁴ Consequently, this produces paradoxically higher relative cerebral blood flow (rCBF) readings within the cortical gray matter ROIs, which must be interpreted strictly as an index of maximal arteriolar vasodilation rather than an actual increase in physiological tissue perfusion.^{2,4} Following successful CAS, immediate restoration of the vascular lumen diameter returns downstream cerebral perfusion pressures to physiological baselines.⁴ Consequently, the chronic stimulus for maximal microvascular dilation is removed, causing the previously over-dilated capillary beds to constrict back to normal dimensions.⁴ This stabilization explains why follow-up CTP examinations performed on the 14-patient subgroup demonstrated a significant postprocedural decrease in rCBV ($p=0.0016$) and rCBF ($p=0.0073$) metrics back toward baseline physiological balances, while concurrently shortening the prolonged transit times (rMTT, $p=0.0001$).^{1,6,9} This post-interventional shift underscores the therapeutic efficacy of CAS in successfully decommissioning chronic hemodynamic strain and re-establishing normal circulatory dynamics.^{2,4}

Although cerebral hyperperfusion syndrome (CHS) remains a well-documented risk following rapid endovascular lumen restoration,¹⁰ none of the 14 patients evaluated postprocedurally in our study developed clinical or radiological signs of CHS. The immediate post-CAS reduction of rCBV and rCBF toward normal thresholds observed in our early (24-48 hours) follow-up group highlights a well-regulated microvascular de-escalation rather than luxury hyperperfusion, validating the protective efficacy of timely intervention.

Furthermore, the lack of a statistically significant correlation between the anatomical stenosis degree and raw baseline

CTP markers deserves attention. This mismatch strongly reinforces the pathophysiological principle that collateral circulatory pathways (such as the circle of Willis and ophthalmic anastomoses) and individual cerebrovascular reserve capacity play a more decisive role in cerebral tissue supply than luminal cross-sectional narrowing alone.^{2,4} Consequently, functional imaging with quantitative CTP may provide complementary haemodynamic information beyond purely anatomical angiographic measurements.

The observed postprocedural improvement in perfusion parameters is consistent with the expected physiological response after successful carotid revascularisation. Restoration of arterial lumen diameter may increase cerebral perfusion pressure and improve distal cerebral blood supply. As a result, cerebral circulation time decreases and perfusion becomes more balanced between the hemispheres. Similar haemodynamic improvements after CAS have been reported in previous CT perfusion studies.^{1,6}

CTP imaging provides quantitative evaluation of cerebral perfusion and enables rapid assessment of regional cerebral haemodynamics.^{7,8} Compared with conventional imaging methods, CT perfusion offers functional information regarding cerebral microcirculation and tissue perfusion. In routine clinical practice, this technique may help identify patients with haemodynamically significant stenosis, determine the severity of cerebral perfusion impairment, and evaluate treatment response following endovascular intervention.^{4,7}

In our study, CBV changes were interpreted within the context of chronic autoregulatory compensation, where reduced perfusion pressure in chronic high-grade carotid stenosis induces distal arteriolar vasodilatation to preserve tissue viability. Consequently, the co-occurrence of prolonged transit times alongside altered relative perfusion indices serves as a robust indicator of critical hemodynamic stress rather than anatomical stenosis severity alone. This distinction highlights that software-quantified CTP parameters successfully capture individual autoregulatory reserve capacities, offering superior functional insights that transcend purely structural angiographic measurements.

Limitations

Several limitations of this study should be acknowledged. First, the retrospective design and relatively small patient population may reduce the generalisability of the findings. Second, follow-up CT perfusion imaging after CAS was available only in a subgroup of patients, limiting comprehensive evaluation of postprocedural haemodynamic changes. Third, long-term neurological outcomes and clinical follow-up data were not assessed. In addition, potential effects of collateral circulation and individual variations in cerebrovascular reserve could not be fully evaluated.

Despite these limitations, the present study demonstrates that CT perfusion imaging can provide valuable information regarding cerebral haemodynamic alterations in patients with carotid artery stenosis. The ability of CT perfusion to quantitatively assess CBF dynamics may contribute to patient selection, evaluation of stenosis severity, and assessment of

treatment response following carotid artery stenting.^{1,6} Future prospective studies with larger patient populations and long-term clinical follow-up are needed to further clarify the role of CT perfusion imaging in the management of carotid artery stenosis and the evaluation of postprocedural cerebral haemodynamic recovery.

CONCLUSION

As a result, severe carotid artery stenosis leads to significant regional cerebral haemodynamic impairment, characterized by prolonged rMTT and altered compensatory rCBF/rCBV parameters. CAS provides measurable and significant immediate improvement in cerebral perfusion by restoring arterial blood supply and enabling the normalization of microvascular autoregulation. CTP imaging serves as a valuable, rapid, and objective modality for preprocedural evaluation and early post-treatment monitoring of haemodynamic recovery in clinical practice.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Medical Ethics Committee of the Faculty of Medicine at Gaziantep University (Date: 26.04.2012, Decision No: 199).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained. This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: AD, AŞ; Design: AD, AŞ; Data Collection: AD; Imaging Analysis: AD; Statistical Analysis: AD, AŞ; Manuscript Preparation: AD; Critical Revision of the Manuscript: AŞ; Final Approval of the Manuscript: All Authors.

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Panoramic radiographic age estimation in Turkish children and adolescents: tooth-and sex-specific modelling using Cameriere's open apex method

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ABSTRACT

Aims: To evaluate panoramic radiographic measurements of individual mandibular teeth as predictors of chronological age (CA) in Turkish children and adolescents, using Cameriere's open apex method, and to assess whether sex-stratified modelling improves predictive accuracy.

Methods: This retrospective cross-sectional study analysed 199 digital panoramic radiographs from Turkish individuals aged 5-14 years (111 females, 88 males). Normalized open apex measurements were obtained for the seven left mandibular permanent teeth. Univariate screening followed by backward elimination was used to construct multiple linear regression models for the overall cohort and stratified by sex. Internal validation was performed using 10-fold cross-validation and bootstrapping with 1000 resamples.

Results: In the overall model, teeth 34 and 37 were retained as significant predictors ($R^2=77.0\%$; standard error of estimate [SEE]=1.06 years; cross-validated $R^2=70.4\%$). The female-specific model retained teeth 34 and 35 ($R^2=78.9\%$; SEE=1.00 year; cross-validated $R^2=69.6\%$). The male-specific model retained teeth 33, 35 and 37 ($R^2=84.0\%$; SEE=0.92 years; cross-validated $R^2=77.8\%$); however, the male subgroup ($n=88$) did not meet Green's recommended sample-size criterion, and the stability of this model is therefore limited. Age-stratified analyses revealed systematic overestimation in the 12-13-year age range across all models.

Conclusion: Individual teeth differed substantially in their predictive contributions, and sex-stratified models showed higher cross-validated performance than the pooled model. The moderate sample size ($n=88$ for the male subgroup), single-centre design and absence of external validation or head-to-head comparison with the classical composite framework (normalized open-apex sum, number of teeth with closed apices and sex) limit the conclusions that can be drawn. The findings are hypothesis-generating and require replication before clinical or forensic application.

Keywords: Radiography, panoramic, age determination by teeth, tooth apex, tooth eruption, forensic dentistry

INTRODUCTION

Panoramic radiography is the imaging modality of choice for non-invasive dental age estimation (DAE) in children, providing a comprehensive view of the developing dentition in a single exposure at a relatively low radiation dose.^{1,2} The technique serves as the substrate for both classical morphological assessment and contemporary computational approaches, including recent automated image-based methods.³ Within this radiographic framework, DAE is regarded as one of the most reliable biological indicators of

age, because dental tissues are resistant to environmental influences and follow a predictable developmental sequence that can be quantified from radiographs.

Among radiographic techniques for paediatric DAE, Cameriere's open apex method, introduced in 2006, has emerged as a widely accepted standard.⁴ The method relies on direct radiographic measurement of the inner-apex distance of the seven left permanent mandibular teeth and applies a



regression formula to estimate chronological age (CA). The classical framework incorporates the sum of normalized open apex ratios, the number of teeth with closed apices (N_0) and sex as predictors.^{4,5} Although initially developed for Italian populations and subsequently adapted into a European formula,⁵ the radiographic method has been recalibrated across populations, often requiring local formulas to achieve acceptable accuracy, with population-specific R^2 values reaching 85-90%.⁶⁻¹⁰

Recent findings have drawn attention to the non-uniform contribution of individual mandibular teeth to age estimation. Galić et al.¹¹ showed that second molars alone explained up to 76% of the age variance, whereas first incisors contributed only 39%, suggesting that tooth-specific modelling may improve predictive accuracy beyond composite indices. This shift toward individual tooth contributions also has practical value. In young individuals, where agenesis, trauma or extractions are common, the absence of certain teeth may render full mandibular analysis unfeasible. This is particularly relevant in the Turkish context, where Decayed, Missing and Filled Teeth (DMFT) scores have been reported as high as 1.9 in 12-year-olds, 6.25 among adolescents aged 9-15 years, and up to 8.1 in younger children, indicating a substantial burden of early dental decay and tooth loss.¹²⁻¹⁴

The present study deliberately departs from the classical composite framework and focuses exclusively on individual tooth-level normalized measurements as predictors. The composite open-apex sum and the number of teeth with closed apices (N_0) collapse tooth-level information into single scalars, which by construction obscures the per-tooth contributions that are the primary object of this study; N_0 is, moreover, derivable from the same normalized measurements, because a normalized value of zero denotes a closed apex, and it is strongly collinear with CA across this paediatric range, so its omission avoids redundancy rather than discarding independent information. This design allows direct identification of the most informative individual teeth and enables flexible tooth-specific regression models for clinical scenarios in which the full set of seven mandibular teeth is unavailable. We acknowledge an apparent tension between this clinical motivation and the present modelling step, which required all seven mandibular teeth to be present so that each tooth's individual contribution could be isolated; the reduced-tooth application is the downstream objective that the derived tooth-specific equations are intended to serve, and is not a property of the development sample itself. We acknowledge that this approach sacrifices the integrative power of composite variables and that its performance should be compared against, rather than assumed to replace, the established framework.

The applicability of Cameriere's method in Türkiye was preliminarily assessed by Gulsahi et al.¹⁵ in 573 children, with root mean square errors of 0.94 years in girls and 1.08 years in boys and an overall trend toward age underestimation. The findings supported the potential utility of the method in Turkish children but emphasised the need for further work to improve local precision and adaptability. Building on this, the present pilot study aims to identify which individual mandibular teeth contribute most to DAE in Turkish children

and adolescents using Cameriere's open apex method, and to determine whether tooth-level and sex-specific approaches warrant further investigation in larger Turkish samples.

METHODS

Ethics

This study was conducted with the approval of the Ethics Committee for Clinical Researches at the Faculty of Medicine, Uşak University (Date: 05.05.2021, Decision No: 08). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Written informed consent for the use of anonymised radiographic data in scientific publications was obtained from the parents or legal guardians of all participants prior to imaging.

Study Design and Setting

This retrospective, cross-sectional study was conducted in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guideline.¹⁶ All data were anonymised prior to analysis. The research was conducted at the Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Uşak University, Uşak, Türkiye.

Sample

Digital panoramic images were retrieved from the archives of the Faculty of Dentistry, Uşak University. A total of 761 images from children aged 5-14 years acquired between 2018 and 2021 were initially screened. Sample selection followed predefined inclusion and exclusion criteria.

The inclusion criteria were: (i) high-quality panoramic images with clear visibility of all seven left mandibular permanent teeth; (ii) age between 5 and 14 years at the time of imaging; (iii) confirmed and verifiable birth and radiograph dates; (iv) normal dental eruption patterns; and (v) no history of dental or skeletal developmental delay. Exclusion criteria were: systemic disease (e.g., endocrine disorders), malnutrition, congenital anomalies, dental anomalies such as fusion, gemination, missing or supernumerary teeth, premature birth, obesity, a history of orthodontic treatment, or extractions in the left mandibular quadrant. Images with inadequate diagnostic quality (low resolution, artefacts, distortion, teeth outside the focal trough, or teeth affected by restorations or endodontic treatment) were also excluded.

On this basis, 562 images were excluded: 37 for poor image quality, 76 for systemic or dental anomalies, 51 for incomplete demographic or clinical records, 31 for a history of orthodontic treatment, 366 for missing or altered teeth precluding valid measurement of all seven mandibular teeth, and one for entirely missing demographic and radiographic data identified during data preparation. The final analytic sample comprised 199 participants. The high exclusion rate (73.9%) introduces a substantial risk of selection bias and yields a highly selected sample that may not fully represent the broader Turkish paediatric population. The majority of exclusions (65.1%) were attributable to missing or altered teeth, itself a reflection of the high DMFT burden reported in Turkish children.¹²⁻¹⁴ The requirement that all seven left

mandibular teeth be present and measurable is inherent to the study's design goal of evaluating each tooth's individual predictive contribution, although this criterion creates a paradox: the very characteristics that motivate flexible, tooth-specific models are also the reason for the large number of exclusions.

The final sample (111 females, 55.8%; 88 males, 44.2%) was determined by case availability. Its adequacy for regression analysis is supported by Green's guideline, which recommends a minimum of 106 subjects to evaluate overall model significance ($N \geq 50 + 8m$) and 111 for testing individual predictors ($N \geq 104 + m$), where $m = 7$.¹⁷ The overall sample ($n = 199$) and the female subgroup ($n = 111$) meet both thresholds; the male subgroup ($n = 88$) falls below both criteria. The male-specific model is therefore statistically underpowered, and its coefficients and fit statistics should be regarded as exploratory and interpreted with corresponding caution.

Eligibility screening was performed by an experienced dentomaxillofacial radiologist (ŞE). CA was calculated in decimal format by subtracting the date of birth from the radiograph date. Sex, age and relevant medical history were recorded from patient records by two independent researchers (DM and DE) prior to radiographic measurements; the same researchers anonymised the dataset so that the examiner remained blinded throughout image analysis. No imputation was performed for missing data.

Image Analysis

Radiographs were acquired in digital format using the Vatech Digital X-ray Imaging System PCH-2500 (Vatech, Seogudong, Korea), following imaging protocols consistent with European Academy of Paediatric Dentistry guidance on clinical indication, patient safety and dose optimisation.¹⁸ Images were saved in high-resolution JPEG format, numerically coded and securely archived. Measurements were performed using ImageJ (National Institutes of Health, Bethesda, MD, USA) on a workstation with a 2.7 GHz dual-core Intel Core i5 processor and a Retina LED monitor at 2560×1600 pixel resolution.

Quantitative assessments focused on the seven left permanent mandibular teeth (teeth 31-37), excluding third molars. Images were analysed by a single examiner (ENK), previously trained and calibrated in the protocol and blinded to participants' CAs and medical histories. Tooth numbering followed the Fédération Dentaire Internationale (FDI) two-digit system. To assess intra-observer reliability, 20 panoramic images were randomly re-evaluated by the same examiner after a two-week interval. The intraclass correlation coefficient (ICC), calculated using a two-way mixed-effects model with single measures (ICC [3.1]), was 0.91, indicating excellent repeatability.¹⁹

For DAE, the method described by Cameriere et al.⁴ was followed. The number of teeth with complete root development (N_0) was recorded. For teeth with open apices, the distance between the inner surfaces of the apex (A_i , $i = 1-5$) was measured. For multi-rooted teeth ($i = 6$ and 7), the sum of inner apex distances was calculated. Each apex measurement

was normalized by dividing by the corresponding tooth length (L_i , $i = 1-7$) to reduce variation due to radiographic magnification or angulation (Figure 1).

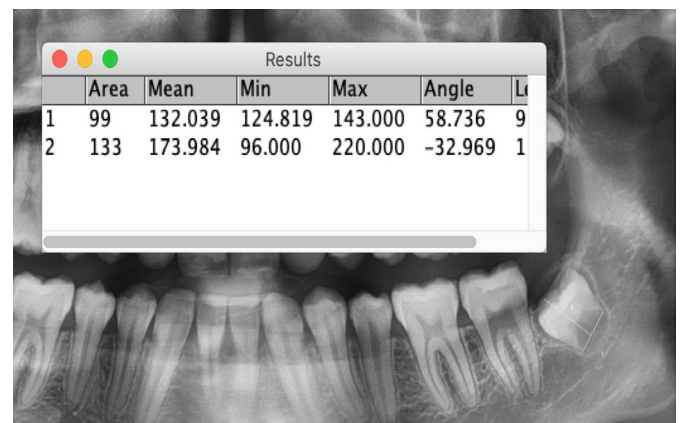


Figure 1. Illustration of Cameriere's open apex method on a panoramic radiograph. Normalized open apex measurements are obtained by dividing the inner-apex distance (A_i) by the corresponding tooth length (L_i) for each of the seven left permanent mandibular teeth, reducing variability due to magnification or angulation

Statistical Analysis

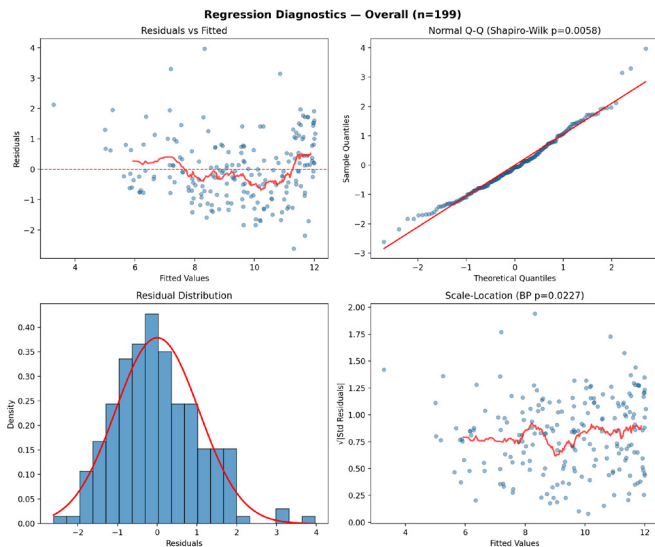
The predictive utility of normalized open apex measurements for estimating CA was assessed using linear regression. CA served as the dependent variable, while the normalized apex-to-root-length ratios of teeth 31-37 were the independent variables. Univariate linear regressions were performed for each tooth. Variables with a p -value < 0.30 in univariate models were entered into a multiple linear regression with backward elimination, with retention at the 0.05 significance level.

Separate models were developed for the overall sample and stratified by sex. R^2 , adjusted R^2 and SEE were calculated for each model. All models were evaluated for compliance with standard assumptions of linear regression: normality of residuals (Shapiro-Wilk test), homoscedasticity (Breusch-Pagan test), multicollinearity (variance inflation factor [VIF]) and independence of residuals (Durbin-Watson statistic). Diagnostic results are reported in the supplementary material (Supplementary Table 1, Supplementary Figure 1-3).

Supplementary Table 1. Summary of regression assumption diagnostics for final models

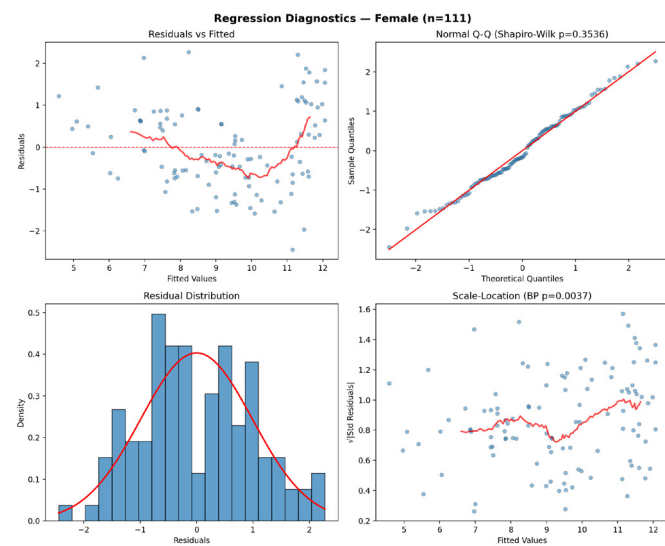
Test	Overall	Female	Male	Threshold	Interpretation
Shapiro-Wilk W	0.9798	0.9869	0.9526		
Shapiro-Wilk p	0.006	0.354	0.003	> 0.05	Residual normality
Breusch-Pagan BP	7.568	11.178	1.795		
Breusch-Pagan p	0.023	0.004	0.616	> 0.05	Homoscedasticity
Durbin-Watson	1.959	2.173	2.081	1.5-2.5	Independence
Shapiro-Wilk tests residual normality (significant $p < 0.05$ indicates non-normal residuals). Breusch-Pagan tests homoscedasticity (significant $p < 0.05$ indicates heteroscedasticity). Durbin-Watson assesses independence of residuals (values within 1.5-2.5 indicate no significant autocorrelation). BP: Breusch-Pagan					

To assess model stability and to estimate optimism in reported metrics, two internal validation procedures were



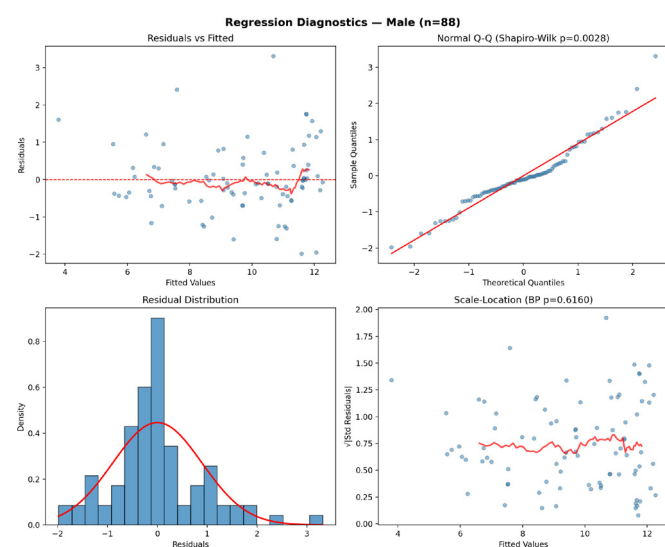
Supplementary Figure 1. Regression diagnostics for the overall model (T34+T37, n=199)

Panels show the residual-versus-fitted plot, the normal Q-Q plot of standardised residuals, the scale-location plot for homoscedasticity assessment and the residual distribution with the fitted normal density



Supplementary Figure 2. Regression diagnostics for the female model (T34+T35, n=111)

Panels show the residual-versus-fitted plot, the normal Q-Q plot of standardised residuals, the scale-location plot for homoscedasticity assessment and the residual distribution with the fitted normal density



Supplementary Figure 3. Regression diagnostics for the male model (T33+T35+T37, n=88)

Note. Panels show the residual-versus-fitted plot, the normal Q-Q plot of standardised residuals, the scale-location plot for homoscedasticity assessment and the residual distribution with the fitted normal density

performed. First, 10-fold cross-validation was conducted with 10 repetitions (100 total folds), reporting the mean and standard deviation of cross-validated R^2 and SEE. Second, bootstrapping with 1000 out-of-bag resamples was used to compute optimism-corrected R^2 values with 95% confidence intervals. A significance level of 5% was adopted throughout.

RESULTS

Sample Characteristics

The final analytic sample comprised 199 participants (111 females, 55.8%; 88 males, 44.2%). Ages ranged from 5.2 to 14.0 years, with a mean CA of 9.43 ± 2.20 years. The distribution by age and sex is presented in Table 1. The 7-9-year age range was best represented ($n=98$; 49.2%), while ages 5-6 and 13-14 contained fewer than 15 participants per group. The age distribution was markedly unbalanced, with a single participant at 14 years and small cell counts in several older groups; the age-stratified error estimates for these sparse strata are correspondingly unstable and should be read as indicative rather than precise.

Table 1. Distribution of participants by age and sex

Age (years)	Female (n)	Male (n)	Total (n)
5	7	6	13
6	6	6	12
7	19	13	32
8	21	5	26
9	24	16	40
10	9	16	25
11	5	13	18
12	12	6	18
13	8	6	14
14	0	1	1
Total	111	88	199

Age groups 5 ($n=13$), 6 ($n=12$), 13 ($n=14$) and 14 ($n=1$) contained fewer than 15 participants. The age-8 group showed marked sex imbalance (21 female, 5 male). These distributional features may limit model reliability in these subgroups

Overall Regression Model

Univariate linear regression analyses identified tooth 34 (T34; mandibular first premolar) as having the highest individual explanatory power ($R^2=75.2\%$; $SEE=1.09$ years), followed by tooth 37 (T37; second molar; $R^2=61.0\%$; $SEE=1.37$ years) and tooth 36 (T36; first molar; $R^2=54.6\%$; $SEE=1.48$ years). In the multiple regression model using backward elimination, T34 and T37 were retained as significant predictors, yielding $R^2=77.0\%$ (adjusted $R^2=76.7\%$) with $SEE=1.06$ years (Table 2). The regression equation for the overall sample was:

$$\text{Age} = 12.09 - (6.72 \times \text{T34}) - (1.15 \times \text{T37})$$

Female-Specific Regression Model

In the female subgroup ($n=111$), both T34 and tooth 35 (T35; second premolar) individually explained over 73% of the variance in univariate models ($R^2=73.3\%$ and 73.2% , respectively; $SEE=1.13$ years for both). In the multivariate model these two teeth were retained, achieving $R^2=78.9\%$

(adjusted $R^2=78.5\%$) with $SEE=1.00$ year (**Table 2**). The regression equation for females was:

$$\text{Age}=12.06-(4.96 \times T34)-(3.59 \times T35) \quad (n=11; p<0.001)$$

Table 2. Univariate and multivariate regression models for dental age estimation, overall and by sex

Tooth	Uni p	Uni R ² (%)	Uni SEE (yr)	Multi p
Overall (n=199); multi R²=77.0%; adj R²=76.7%; SEE=1.06 yr				
Tooth 31	0.054	1.9	2.17	-
Tooth 32	<0.001	11.8	2.06	-
Tooth 33	0.654	0.1	2.19	-
Tooth 34	<0.001	75.2	1.09	<0.001
Tooth 35	<0.001	32.4	1.80	-
Tooth 36	<0.001	54.6	1.48	-
Tooth 37	<0.001	61.0	1.37	<0.001
Female (n=111); multi R²=78.9%; adj R²=78.5%; SEE=1.00 yr				
Tooth 31	0.021	4.9	2.13	-
Tooth 32	<0.001	44.4	1.63	-
Tooth 33	0.712	0.1	2.18	-
Tooth 34	<0.001	73.3	1.13	<0.001
Tooth 35	<0.001	73.2	1.13	<0.001
Tooth 36	<0.001	57.5	1.42	-
Tooth 37	<0.001	49.7	1.55	-
Male (n=88); multi R²=84.0%; adj R²=83.4%; SEE=0.92 yr				
Tooth 31	0.053	4.4	2.17	-
Tooth 32	0.002	11.4	2.09	-
Tooth 33	<0.001	72.5	1.17	<0.001
Tooth 34	<0.001	78.8	1.02	-
Tooth 35	<0.001	15.1	2.05	0.017
Tooth 36	<0.001	52.7	1.53	-
Tooth 37	<0.001	77.6	1.05	<0.001

R²: Coefficient of determination, SEE: Standard error of estimate, Uni: Univariate, Multi: Multivariate (backward elimination), Adj: Adjusted, - = not retained in the final model. Multi R², Adj R² and SEE in group headers refer to the final multivariate model for each subgroup

Male-Specific Regression Model

In the male subgroup (n=88), T34 was the strongest univariate predictor ($R^2=78.8\%$; $SEE=1.02$ years), followed by T37 ($R^2=77.6\%$; $SEE=1.05$ years) and tooth 33 (T33; mandibular canine; $R^2=72.5\%$; $SEE=1.17$ years). The backward elimination

model retained three predictors, T33, T35 and T37, achieving $R^2=84.0\%$ (adjusted $R^2=83.4\%$) with $SEE=0.92$ years (**Table 2**). The regression equation for males was:

$$\text{Age}=12.45-(5.67 \times T33)+(0.64 \times T35)-(2.69 \times T37) \quad (n=88; p<0.001)$$

Although T34 was the strongest univariate predictor in males ($R^2=78.8\%$), it was not retained in the multivariate model. Backward elimination evaluates partial contributions conditional on the other retained predictors, and the predictive variance of T34 is largely captured by the combination of T33 and T37, rendering its independent contribution non-significant after adjustment. The positive coefficient for T35 ($B=0.64$; $p=0.017$) likely reflects a suppressor effect: after accounting for the negative contributions of T33 and T37, the residual variance in T35 captures developmental timing information that would otherwise be confounded. We emphasise, however, that a positive coefficient of this kind is biologically counterintuitive and may equally represent a dataset-specific artefact arising from the modest male sample and the particular collinearity structure of this cohort; it should therefore be interpreted with caution and requires confirmation in independent data before any developmental interpretation is accepted. VIF values for all three predictors remained within acceptable limits ($VIF \leq 2.92$), indicating that these patterns are not multicollinearity artefacts.

Summary of Final Model Coefficients

Regression coefficients and collinearity diagnostics for all final models are presented in **Table 3**.

Internal Validation

Results of 10-fold cross-validation (repeated 10 times) and bootstrap validation (1000 out-of-bag resamples) are summarised in **Table 4**. The cross-validated R^2 values showed moderate optimism relative to apparent R^2 in all models (optimism range: 6.2-9.3 percentage points). The male model demonstrated the highest validated performance (cross-validated $R^2=77.8\%$; bootstrap-corrected $R^2=80.4\%$), followed by the female model (75.6%) and the overall model (72.9%). The large standard deviations of cross-validated R^2 (15.3-25.4%) reflect considerable fold-to-fold variability, particularly in the female model ($SD=25.4\%$), indicating that predictive performance is sensitive to sample composition in datasets of this size.

Table 3. Regression coefficients for all final models

Model	Variable	B	SE	t	p	VIF	Tolerance
Overall	Intercept	12.086	0.132	91.779	<0.001	-	-
	T34	-6.723	0.569	-11.823	<0.001	2.673	0.374
	T37	-1.145	0.253	-4.524	<0.001	2.673	0.374
Female	Intercept	12.057	0.168	71.845	<0.001	-	-
	T34	-4.958	0.897	-5.528	<0.001	3.651	0.274
	T35	-3.588	0.666	-5.388	<0.001	3.651	0.274
Male	Intercept	12.455	0.173	72.127	<0.001	-	-
	T33	-5.665	0.902	-6.279	<0.001	2.917	0.343
	T35	0.642	0.263	2.441	0.017	1.448	0.691
	T37	-2.686	0.333	-8.072	<0.001	2.598	0.385

B: Unstandardised regression coefficient, SE: Standard error, VIF: Variance inflation factor. All VIF values <5.0 and all tolerances >0.20, indicating acceptable multicollinearity levels. t-values were computed from unrounded coefficients; minor discrepancies may arise when recalculating from the rounded B and SE values presented here

Table 4. Internal validation of regression models

Model	Apparent R ²	CV R ² (SD)	CV SEE	Boot R ²	Boot R ² 95% CI	Corrected R ²
Overall	77.0%	70.4% (15.3%)	1.11	72.9%	(56.4%; 82.7%)	72.9%
Female	78.9%	69.6% (25.4%)	1.01	75.6%	(62.0%; 84.3%)	75.6%
Male	84.0%	77.8% (20.5%)	0.90	80.4%	(65.8%; 89.5%)	80.4%

CV= 10-fold cross-validation (100 total folds); Boot=Bootstrap (1000 out-of-bag resamples), Corrected R²= Optimism-corrected, SEE in years, SD: Standard deviation across folds. CV: Cardiovascular, SEE: Standard error of estimate, CI: Confidence interval

Regression Assumption Diagnostics and Age-Stratified Performance

Regression assumption diagnostics are reported in the supplementary material (**Supplementary Table 1**, **Supplementary Figure 1-3**). The female and overall models showed significant heteroscedasticity (Breusch-Pagan $p < 0.05$), indicating non-uniform prediction error variance across the age range; the male model satisfied all assumptions. Age-stratified analysis revealed underestimation in younger children (ages 5-9), a transition zone near ages 10-11 where prediction errors approached zero, and progressive overestimation in older children (ages 12-13). In the overall model, mean prediction error ranged from -0.47 years (age 7-8) to +1.58 years (age 13). This pattern is consistent with the diminishing predictive value of open apex measurements as teeth approach root closure. The systematic overestimation at ages 12-13, observed across all three models, indicates deterioration of model calibration toward the upper end of the studied range and may constrain clinical applicability in older adolescents, in whom open-apex information is least informative. Age-stratified results for all three models are provided in supplementary **Supplementary Table 2-4** and **Supplementary Figure 4**; predicted-versus-actual age scatter plots for all three models are shown in **Supplementary Figure 5**.

Supplementary Table 2. Age-stratified prediction errors for the overall model (n=199)

Age	n	Mean error (yr)	SD (yr)	MAE (yr)	RMSE (yr)
5	13	-0.136	0.834	0.661	0.812
6	12	-0.288	0.880	0.744	0.891
7	32	-0.470	0.808	0.783	0.924
8	26	-0.474	1.044	0.906	1.128
9	40	-0.336	0.918	0.796	0.966
10	25	-0.029	1.022	0.729	1.001
11	18	0.307	0.582	0.459	0.643
12	18	0.889	0.860	0.889	1.220
13	14	1.576	0.264	1.576	1.596

MAE: Mean absolute error, RMSE: Root mean square error. Negative mean error indicates age underestimation; positive indicates overestimation

Supplementary Table 3. Age-stratified prediction errors for the female model (n=111)

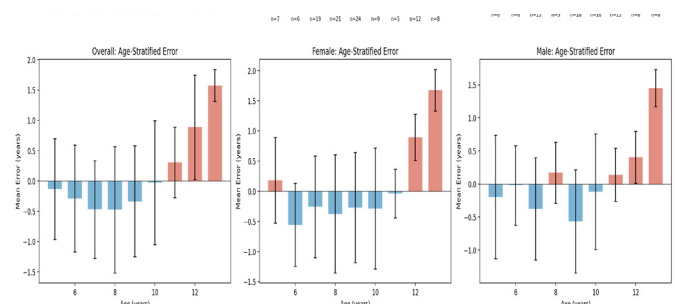
Age	n	Mean error (yr)	SD (yr)	MAE (yr)	RMSE (yr)
5	7	0.180	0.711	0.610	0.682
6	6	-0.556	0.690	0.639	0.840
7	19	-0.257	0.845	0.791	0.862
8	21	-0.375	0.979	0.866	1.027
9	24	-0.273	0.915	0.749	0.936
10	9	-0.285	1.000	0.790	0.985
11	5	-0.036	0.406	0.335	0.365
12	12	0.894	0.382	0.894	0.966
13	8	1.675	0.344	1.675	1.705

SD: Standard deviation, MAE: Mean absolute error, RMSE: Root mean square error. Negative mean error indicates age underestimation; positive indicates overestimation

Supplementary Table 4. Age-stratified prediction errors for the male model (n=88)

Age	n	Mean error (yr)	SD (yr)	MAE (yr)	RMSE (yr)
5	6	-0.196	0.934	0.731	0.875
6	6	-0.020	0.602	0.467	0.550
7	13	-0.377	0.775	0.660	0.834
8	5	0.173	0.461	0.292	0.447
9	16	-0.565	0.780	0.769	0.943
10	16	-0.117	0.876	0.558	0.856
11	13	0.138	0.402	0.253	0.410
12	6	0.405	0.394	0.427	0.542
13	6	1.451	0.281	1.451	1.474

SD: Standard deviation, MAE: Mean absolute error, RMSE: Root mean square error. Negative mean error indicates age underestimation; positive indicates overestimation. The systematic overestimation in the 12-13 age range is consistent with reduced predictive value of open apex measurements as teeth approach root closure

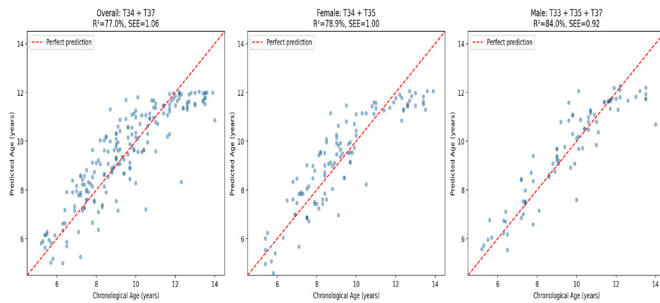
**Supplementary Figure 4.** Scatter plots of predicted versus chronological age for all three models

Each panel displays predicted age (y-axis) against chronological age (x-axis): overall (left), female (centre) and male (right). The dashed line represents the identity ($y=x$); points above the line indicate overestimation and points below indicate underestimation

DISCUSSION

Cameriere's open apex method has become one of the most widely employed radiographic techniques for DAE in children since its introduction in 2006.²⁰ Initially developed using Italian datasets, subsequent research has emphasised the need to adapt the method to specific populations and anatomical contexts.⁶⁻¹⁰ The present study departs from the classical framework, which uses composite variables (sum of normalized open apices, N_0 and sex) as predictors, and evaluates individual tooth-level normalized measurements

instead, building models from the most informative teeth. This approach enables identification of the teeth that carry the greatest predictive weight (information obscured by composite indices) and responds to the clinical reality of high DMFT burden in Turkish children.¹²⁻¹⁴ The trade-off is the loss of the integrative power of composite variables, and a



Supplementary Figure 5. Mean prediction error by age group for all three models

Mean prediction error (predicted age minus chronological age, in years) is plotted against age group for the overall, female and male models. Positive values indicate overestimation and negative values indicate underestimation; the horizontal line at zero marks perfect prediction. The systematic overestimation observed in the 12–13-year age range across all models reflects the diminishing predictive value of open apex measurements as teeth approach root closure

head-to-head comparison against the classical framework in the same sample would be a valuable extension.

Within this framework, the male-specific model ($R^2=84.0\%$; cross-validated $R=77.8\%$; $SEE=0.92$ years) retained T33, T35 and T37 and showed the highest cross-validated performance among the three models. This result must be interpreted with caution because the male subgroup ($n=88$) falls below Green's recommended minimum sample size,¹⁷ and the cross-validated R^2 SD of 20.5% indicates substantial fold-to-fold instability. The higher male performance may reflect the complementary developmental timing of the canine (T33) and the second molar (T37), which together span a wider window of root maturation than the premolar pair (T34+T35) retained in the female model, but this interpretation requires confirmation in independent samples. Taken together, the underpowered subgroup, the wide cross-validation variability and the absence of any head-to-head comparison with the classical composite model mean that the apparent advantage of the male model should be read as a preliminary observation and not as evidence of established superiority.

In the female-specific model, the combination of T34 and T35 yielded $R^2=78.9\%$ (cross-validated $R^2=69.6\%$) with $SEE=1.00$ year. Previous studies have emphasised higher reliability of age estimation in females within this age range, attributed to earlier onset and more regular progression of dental maturation.¹⁵ The meta-analysis by Hostiuc et al.²¹ similarly reported slightly better accuracy in females across Cameriere-based studies, though differences were not statistically significant. In the present sample, however, the male model showed higher cross-validated R^2 ; given the smaller male subgroup and wider confidence intervals, this finding should be regarded as preliminary.

The overall model (T34+T37; $R^2=77.0\%$; cross-validated $R^2=70.4\%$; $SEE=1.06$ years) demonstrated adequate performance. The sex-stratified models yielded higher cross-validated R^2 values, consistent with the hypothesis that sex-specific modelling may be beneficial, although the magnitude of improvement varied and the comparison is limited by differing subgroup sizes. Because the classical composite framework was not fitted to the same data, the present results speak to the relative behaviour of the tooth-specific models among themselves and cannot support any claim of superiority or added value over the established Cameriere method; such a claim would require a direct comparison within an identical sample.

Among studies applying Cameriere's method to Turkish children, most employed the European regression formula without local modification.^{15,22,23} Özdemir Tosyaloğlu et al.²⁴ developed a Turkish-specific formula integrating dental and skeletal indicators, achieving 72.8% accuracy. The cross-validated performance of the male (77.8%) and female (69.6%) models in the present study falls in a comparable range, although differences in design, sample composition and predictor selection preclude direct comparison.

Consistent with previous tooth-specific work, the individual tooth analyses confirmed that mandibular premolars and the second molar are among the most reliable indicators for CA estimation.^{11,25,26} The emergence of the canine (T33) as a key predictor exclusively in the male model is noteworthy and may reflect sex-based differences in canine developmental timing. Although T37 played a significant role in both the overall and male models, its exclusion from the female model is consistent with its later and more variable maturation pattern.

From a radiographic standpoint, the present findings should be situated within the broader landscape of imaging-based DAE. Panoramic radiography remains the reference modality for paediatric DAE owing to its broad anatomical coverage, low radiation dose and routine availability in dental practice.¹⁸ Cone-beam computed tomography offers higher-resolution three-dimensional visualisation of root and apex anatomy but is not justified for age estimation alone given its higher dose. Recent deep learning approaches on panoramic radiographs report mean absolute errors of approximately 1 year,³ comparable to the SEE values obtained here (0.92–1.06 years), so measurement-based methods retain value as interpretable benchmarks for automated models. Standardised acquisition geometry, positioning and digital image-analysis workflows therefore remain central to reproducibility in panoramic radiographic age estimation.

Limitations

The high exclusion rate (73.9%) and single-centre design limit generalisability. The final sample ($n=199$; 55.8% female) showed uneven age-sex distributions (e.g., age 8: 21F/5M; age 14: $n=1$), and the requirement for seven intact mandibular teeth inherently excludes the high-DMFT population these models aim to serve.^{12–14} Systematic overestimation emerged at ages 12–13 (up to +1.58 years), reflecting diminished open apex variability near root closure.^{15,27} Significant heteroscedasticity (female and overall models) and residual non-normality (overall and male models) warrant cautious interpretation of standard errors. Under these violations the ordinary least-squares coefficients remain unbiased, but the model-based standard errors, confidence intervals and p-values are no longer fully reliable, so the significance tests for individual predictors should be read conservatively. The heteroscedasticity observed here is age-dependent, with prediction error variance increasing as teeth approach root closure, which parallels the age-stratified bias described above. For this reason we place greater weight on the bootstrap confidence intervals, which are distribution-free and therefore more robust to non-normality and non-constant variance, and on the optimism-corrected R^2 values than on the model-based inference; weighted or robust-variance regression and variance-stabilising transformations

are natural next steps in larger samples. Backward elimination, while useful for exploratory predictor selection, is susceptible to overfitting and model instability; the resulting models are hypothesis-generating, not confirmatory. The omission of classical composite variables (sum of normalized apices, No and sex) precludes direct comparison with the established Cameriere framework. Panoramic imaging limitations further constrain anterior tooth measurements due to focal trough geometry, and early apex closure of teeth 31, 32 and 36 (around ages 8-9) restricts their utility in older children.²⁸ External validation in larger, multicentre Turkish samples is essential before forensic or clinical application.

CONCLUSION

This exploratory pilot study evaluated panoramic radiographic measurements of individual mandibular teeth for DAE in Turkish children and adolescents using Cameriere's open apex method. As a preliminary observation, the sex-stratified models yielded higher cross-validated R^2 values than the pooled model and identified distinct predictor sets (male: T33, T35 and T37; cross-validated $R^2=77.8\%$; SEE=0.92 years; female: T34 and T35; cross-validated $R^2=69.6\%$; SEE=1.00 year); this pattern should be regarded as hypothesis-generating rather than as evidence of superior performance. The moderate sample size (particularly $n=88$ for males), high exclusion rate, single-centre design, assumption violations in two of three models, absence of comparison with the classical composite framework and systematic overestimation at older ages collectively limit these findings to hypothesis-generating status. External validation in larger, multicentre Turkish samples, head-to-head comparison with composite Cameriere models, and benchmarking against deep learning approaches operating on panoramic radiographs are necessary before any clinical or forensic application can be considered.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Ethics Committee for Clinical Researches at the Faculty of Medicine, Uşak University (Date: 05.05.2021, Decision No: 08).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained. This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: ENK, ŞE, AG, ILAR, RC; Design: ENK, ŞE, AG, ILAR, RC; Control: ENK, ŞE, AG, ILAR, RC; Resources: ENK, ŞE, AG, ILAR, RC; Materials: ENK, ŞE, AG, ILAR, RC; Data Collection and/or Processing: ENK, ŞE, AG, ILAR, RC; Analysis and/or Interpretation: ENK, ŞE, AG, ILAR, RC; Literature Review: ENK, ŞE, AG, ILAR, RC; Writing the Article: ENK, ŞE, AG, ILAR, RC; Critical Review: ENK, ŞE, AG, ILAR, RC.

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Covered stent placement in interventional radiology: a single-center experience

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ABSTRACT

Aims: This study aimed to retrospectively evaluate the technical and clinical outcomes of covered stent applications in interventional radiology practice.

Methods: Seventeen patients (10 male, 7 female; mean age: 54.1±16.9 years) who underwent covered stent placement for pseudoaneurysm (PA) and/or arteriovenous fistula (AVF) between January 2018 and December 2024 were retrospectively analyzed. Patients were categorized into two groups according to the underlying etiology: Group 1 (post-hepatopancreatobiliary [HPB] surgery, n=7) and group 2 (post-trauma and iatrogenic injury, n=10). Technical success, clinical success, complication rate, and 30-day mortality were assessed.

Results: Technical and clinical success rates were 100% in all patients. The mean procedural time was 36.6±11.1 minutes. One patient (5.9%) developed a major complication (sepsis). The 30-day mortality rate was 5.9% (1/17); this patient had undergone HPB surgery. A statistically significant difference was found between the groups regarding age (p=0.044), while hemoglobin levels did not differ significantly (p=0.968).

Conclusion: Covered stent placement is a safe and effective method with high technical and clinical success rates for the treatment of both visceral and peripheral PAs and AVFs. Interventional radiology may be considered a first-line treatment option in appropriately selected patients.

Keywords: Covered stent, pseudoaneurysm, arteriovenous fistula, interventional radiology, endovascular treatment

INTRODUCTION

Pseudoaneurysms (PAs) and arteriovenous fistulas (AVFs) are among the vascular complications frequently encountered in interventional radiology practice. These lesions may arise following surgical interventions, iatrogenic vascular injuries, and penetrating trauma. Minimally invasive endovascular treatment modalities are increasingly preferred in patients with high surgical mortality and morbidity risk.^{1,2}

PAs developing after hepatopancreatobiliary (HPB) surgery are well-known vascular complications, particularly associated with pancreaticoduodenectomy and distal pancreatectomy. The coexistence of pancreatic fistula, abscess, and recurrent hemorrhage complicates management in these cases.^{3,4} Peripheral PAs most commonly develop following cardiac and peripheral angiography procedures, hemodialysis catheter placement, or penetrating trauma.^{5,6}

Covered stents (stent grafts) are endovascular implants that exclude PA or AVF flow while preserving the parent vessel lumen. They are manufactured in two main types: balloon-expandable (BE) and self-expandable (SE), coated with polytetrafluoroethylene (PTFE) or Dacron over a nitinol or cobalt-chromium scaffold.^{7,8} Technical success rates of 80-100% have been reported for covered stent use in visceral artery PAs.^{9,10} High success and low complication rates have also been achieved in the treatment of peripheral arterial PAs and AVFs.^{11,12}

This study aimed to retrospectively evaluate patients who underwent covered stent placement for PA and AVF of various etiologies at our center. Primary endpoints were technical success, clinical success, and complication rates.

METHODS

Ethics

This study was conducted with the approval of the Clinical Researches Ethics Committee of the Dışkapı Yıldırım Beyazıt Training and Research Hospital, University of Health Sciences (Date: 29.04.2019, Decision No: 62/27). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Patient Selection

This study was conducted as a single-center, retrospective cohort study. A total of 17 consecutive adult patients who underwent coated stent implantation for PA and/or AVF between January 2018 and December 2024 were included in the study. Informed consent was obtained from all patients.

Imaging and Procedural Protocol

All patients were evaluated with computed tomography angiography (CTA) prior to the procedure. PA dimensions, parent artery origin, presence of fistulous tract, and additional complications (abscess, pancreatic fistula) were recorded. Procedures were performed under digital subtraction angiography (DSA) guidance. Appropriately sized covered stents (stent diameter 1-2 mm larger than the parent artery) were selected based on the location and diameter of the parent artery. BE covered stents were preferred for visceral arteries (hepatic artery, superior mesenteric artery) requiring high radial force, while SE covered stents were used in peripheral and tortuous vessels requiring flexibility. BE covered stents used in visceral artery cases included the iCover (iVascular, Barcelona, Spain) device. SE covered stents used in peripheral cases included the Viabahn (W.L. Gore & Associates, Flagstaff, AZ, USA) device. All patients received intraoperative systemic heparinization (70 IU/kg). Post-procedurally, dual antiplatelet therapy (aspirin 100 mg/day+clopidogrel 75 mg/day) was prescribed for a minimum of one month, followed by aspirin monotherapy indefinitely, per institutional protocol.

Definitions of Technical and Clinical Success

Technical success was defined as complete exclusion of the PA/AVF with preservation of main vessel flow on completion angiography. Clinical success was defined as cessation of active hemorrhage confirmed on completion angiography, hemodynamic stabilization within 24 hours post-procedure, absence of reintervention or surgical rescue during the index hospitalization, and no recurrent bleeding episode during the available follow-up period. Major complication was classified as any event requiring sepsis management, organ failure support, or additional surgical/endovascular reintervention.

Statistical Analysis

The data were performed using IBM SPSS Statistics version 26.0. Continuous variables were expressed as mean±standard deviation (SD), and categorical variables as counts and percentages. Independent samples t-test was used to compare continuous variables between two groups. A p-value <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

Seventeen patients were included: 10 male (58.8%) and 7 female (41.2%), with a mean age of 54.1±16.9 years (range: 27-82 years). Patients were categorized into two groups according to the underlying etiology: Group 1 consisted of 7 PA/AVF cases following HPB surgery (subtotal gastrectomy n=1, HPB surgery n=6). Group 2 comprised 10 cases following trauma (stab wound, gunshot injury) or iatrogenic intervention (angiography puncture, dialysis catheter placement).

The mean pre-procedure hemoglobin level was 8.14±1.45 g/dl (range: 5.3-11.2 g/dl); all patients were anemic. The mean time from symptom onset to procedure was 15.9±16.6 days (median: 9.0 days, range: 2-60 days). The mean PA size was 10.8±13.0 mm (median: 7.0 mm, range: 2.5-55 mm). A statistically significant difference was found between the groups for age (group 1: 63.7±11.7 vs. group 2: 47.3±17.1 years; p=0.044) and time from symptom onset to procedure (27.7±17.4 vs. 7.7±7.0 days; p=0.005), the latter reflecting the more complex preoperative course in HPB surgery patients often complicated by concurrent pancreatic fistula or abscess. No statistically significant difference was observed regarding PA size (17.3±17.0 vs. 6.4±2.4 mm; p=0.061), procedure duration (32.4±13.4 vs. 39.7±9.2 min; p=0.201), or hemoglobin levels (8.16±1.12 vs. 8.13±1.70 g/dl; p=0.968). Comparative demographic data are presented in **Table 1**.

Table 1. Comparative demographic and procedural characteristics by group

Variable	Group 1: hepatobiliary (n=7)	Group 2: trauma/iatrogenic (n=10)	p-value
Age, mean±SD (years)	63.7±11.7	47.3±17.1	0.044
Sex (M/F)	5M/2F	5M/5F	-
Pre-procedure Hgb (g/dl)	8.16±1.12	8.13±1.70	0.968
Time from symptom to procedure (days)	27.7±17.4	7.7±7.0	0.005
PA size (mm)	17.3±17.0	6.4±2.4	0.061
Procedure duration (min)	32.4±13.4	39.7±9.2	0.201
Technical success	100%	100%	-
Clinical success	100%	100%	-
30-day mortality	1 (14.3%)	-	-

SD: Standard deviation, M/F: Male/female, Hgb: Hemoglobin, PA: Pseudoaneurysm, Min: Minute

Technical Characteristics

Regarding the distribution of parent arteries, visceral arteries included the hepatic artery (n=4, 23.5%) and superior mesenteric artery (n=3, 17.6%) (**Figure 1**). Peripheral arteries included the femoral arteries (right/left SFA n=3, right/left DFA n=2), brachial artery (n=1), axillary artery (n=1), vertebral artery (n=1), radial arteries (n=2), and right carotid artery (n=1) (**Figure 2**). The femoral approach was the most commonly used access site (76.5%, 13/17). Left brachial access was preferred in two patients (11.8%) in whom the lesion anatomy made femoral approach unsuitable.

Regarding stent type, 10 patients (58.8%) received a BE covered stent, and 7 patients (41.2%) received a SE covered

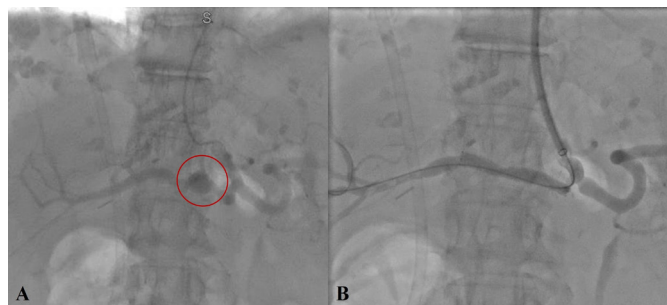


Figure 1. An 82-year-old female patient with pseudoaneurysm (PA) of the common hepatic artery following hepatobiliary surgery

(A) Digital subtraction angiography (DSA) image demonstrating the PA arising from the common hepatic artery. (B) Post-procedure DSA confirms complete exclusion of the PA following covered stent placement, with preserved patency of the hepatic artery



Figure 2. A 48-year-old female patient with right vertebral artery injury sustained during temporary cervical catheter insertion

(A, B) Digital subtraction angiography (DSA) images demonstrating a pseudoaneurysm (PA) at the origin of the right vertebral artery. (C) Fluoroscopic image showing covered stent placement at the lesion site. (D) Post-procedure DSA confirms complete patency of the right vertebral artery with full exclusion of pathological filling

stent. BE covered stents were exclusively used in visceral arteries, while SE covered stents were selected at peripheral locations requiring flexibility and conformability (**Figure 3**). Regarding diagnostic catheters used: Vertebral (n=6), Cobra 2 (n=5), SIM 1 (n=4), SIM 2 (n=2).

Technical Success, Clinical Success, Complications, and Mortality

Technical and clinical success were achieved in all patients (100%). The mean procedure time was 36.6 ± 11.1 minutes (group 1: 32.4 ± 13.4 min; group 2: 39.7 ± 9.2 min). One patient (5.9%) developed post-procedure sepsis as a major complication; this was a 63-year-old female patient with SMA PA and pancreatic fistula in whom technical success was achieved, but the underlying infectious process persisted and progressed to sepsis. The overall 30-day mortality rate was 5.9% (1/17). The deceased patient was a 60-year-old male HPB surgery patient with a triad of SMA PA, pancreatic fistula, and abscess; despite technical success, he died due to infectious complications and multi-organ failure. Individual patient data are summarized in **Table 2**.

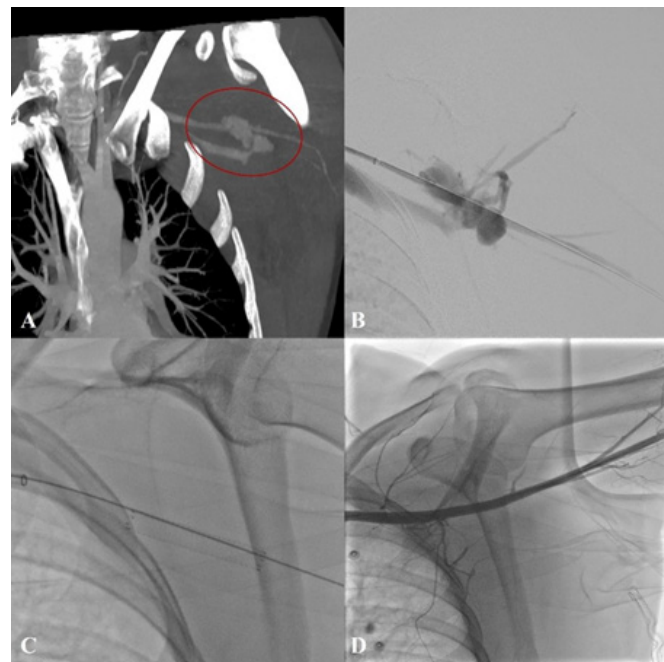


Figure 3. A 27-year-old male patient with stab wound injury

(A) Volume rendering computed tomography angiography (CTA) image demonstrates pseudoaneurysm (PA) and arteriovenous fistula (AVF) arising from the left axillary artery (red circle). (B) Digital subtraction angiography (DSA) image confirming the PA and AVF prior to intervention. (C) Fluoroscopic image demonstrating self expandable covered stent delivery across the lesion. (D) Post-procedure Digital subtraction angiography (DSA) confirms complete exclusion of the PA and AVF with full patency of the axillary artery and its distal branches

DISCUSSION

In this study, a 100% technical and clinical success rate was achieved in the endovascular treatment of PAs and AVFs using covered stents across both visceral and peripheral anatomical distributions. This high success rate is consistent with previous reports and suggests the feasibility of covered stent use across different anatomical locations.

The treatment of visceral PA/AVFs developing after HPB surgery is technically challenging due to coexisting complications such as pancreatic fistula, abscess, or hemobilia. Pedersoli et al.³ reported an 82.8% technical success rate with stent graft placement for hepatic artery PAs following pancreaticoduodenectomy. In our HPB group, technical success was 100%; however, the higher 30-day mortality (14.3%) in this group reflects the complexity of the underlying disease and multi-organ involvement. The death in the SMA PA case, despite technical success, was related to uncontrolled retroperitoneal infection. This finding has been similarly reported by Venturini et al.¹⁴ in their visceral aneurysm stent graft series.

The majority of peripheral PAs and AVFs are of iatrogenic origin. Cardiac and peripheral angiography procedures currently constitute the most common cause of iatrogenic PAs; large sheath size, anticoagulation, and inadequate compression are among the risk factors.^{5,6} Thalhammer et al.⁵ reported technical success in 26/29 cases (89.7%) in their series evaluating covered stent use for femoral PA and AVF treatment. Similar success rates were achieved in the iatrogenic group of the present study, with 100% technical success across the entire series.

In a series evaluating PAs of the superior mesenteric artery, immediate technical success was achieved in all 6 patients,

Table 2. Individual patient clinical and procedural data

No	Etiology	Age	Sex	Parent artery	PA (mm)	Stent type	Time (min)	Complication	Mortality
1	Subtotal gastrectomy	64	M	HA (extrahepatic)	6	Balloon-expandable	55	-	-
2	HPB surgery	64	M	HA (extrahepatic)	30	Balloon-expandable	22	-	-
3	HPB surgery	60	M	SMA	55	Balloon-expandable	34	-	Yes
4	HPB surgery	43	M	HA (extrahepatic)	4	Balloon-expandable	36	-	-
5	HPB surgery	82	F	HA (extrahepatic)	13	Balloon-expandable	15	-	-
6	HPB surgery	63	F	SMA	7	Balloon-expandable	40	Major (Sepsis)	-
7	HPB surgery	70	M	SMA	6	Balloon-expandable	25	-	-
8	Stab wound	27	M	Left axillary artery	5	Self-expandable	30	-	-
9	Dialysis catheter	48	F	Right vertebral artery	4	Balloon-expandable	36	-	-
10	Angiography	72	F	Right SFA	8	Self-expandable	42	-	-
11	Angiography	58	F	Right DFA	7	Balloon-expandable	28	-	-
12	Coronary angiography	32	M	Left radial artery	3.5	Self-expandable	40	-	-
13	Angiography	47	M	Left brachial artery	7	Self-expandable	35	-	-
14	Dialysis catheter	64	F	Right carotid artery	5	Self-expandable	48	-	-
15	Angiography	66	F	Right SFA	10	Self-expandable	34	-	-
16	Stab wound	29	M	Right radial artery	2.5	Self-expandable	47	-	-
17	Gunshot wound	30	M	Right DFA	10	Balloon-expandable	56	-	-

PA: Pseudoaneurysm, min: Minute, M: Male, F: Female, HA: Hepatic artery, HPB: Hepatopancreatobiliary, SMA: Superior mesenteric artery, SFA: Superficial femoral artery, DFA: Deep femoral artery

with long-term patency maintained in the majority.¹³ Venturini et al.,⁷ in a comparative study of covered stenting versus coil embolization in 100 patients, reported significantly higher long-term patency rates in the stent graft group. These findings support the preference for covered stents in lesions with wide necks where flow continuity must be maintained.

Stent type selection is a key determinant of effective treatment. BE stents are preferred for short, necked, and visceral artery lesions owing to their high radial force and precise sizing capability. SE stents offer advantages in peripheral and tortuous arteries due to their flexibility and conformability.^{7,15} In our series, this distinction was appropriately applied: BE covered stents were exclusively used in visceral cases, while SE covered stents were predominantly used in peripheral cases.

Regarding procedure time, the mean 36.6 minutes observed in our series is relatively short. The fact that group 1 (32.4 min) had a shorter procedure time than group 2 (39.7 min) may be explained by the tortuosity and small vessel diameter of peripheral arteries complicating navigation. Among the main complications associated with covered stent placement are stent migration, kinking, thrombosis, and disruption of graft integrity.^{8,10} None of these were observed in our series; the only major complication was a sepsis case related to the underlying infectious process.

Limitations

The main limitations of this study include its retrospective design, relatively small sample size, and single-center experience. Due to the small sample size, particularly in the HPB surgery group, the statistical power of between-group comparisons is limited, and the findings should be interpreted accordingly. Larger multicenter prospective studies are needed to confirm these results. The inability

to obtain systematic long-term patency follow-up data limits the interpretation of results. Nevertheless, this series covering heterogeneous anatomical distributions provides an important contribution documenting the broad-spectrum use of covered stents in interventional radiology practice. Long-term stent patency, thrombosis, and reintervention rates are critical outcome measures that could not be fully assessed in this retrospective series due to inconsistent imaging follow-up. Published series report primary patency rates of 70-90% at 12 months for covered stents in visceral and peripheral arteries, with antiplatelet therapy being a key determinant of long-term outcomes. Future prospective studies with standardized follow-up imaging protocols are warranted to define long-term durability in this patient population.

CONCLUSION

Covered stent placement represents a technically feasible and clinically effective endovascular approach for the management of both visceral and peripheral PAs and AVFs, with high procedural success rates demonstrated in this single-center series. However, given the retrospective design, limited sample size, and absence of systematic long-term follow-up, these findings should be interpreted with caution. Prospective multicenter studies with standardized outcome assessment are needed to further define the role of covered stents in this clinical setting.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted with the approval of the Clinical Researches Ethics Committee of the Dışkapı Yıldırım Beyazıt Training and Research Hospital, University of Health Sciences (Date: 29.04.2019, Decision No: 62/27).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained. This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The author declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

The author is solely responsible for the conception, data collection, analysis, and writing of this manuscript.

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Pseudomyxoma peritonei secondary to appendiceal mucocoele: a case report with characteristic imaging findings

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ABSTRACT

Pseudomyxoma peritonei (PMP) is a rare disease characterized by progressive accumulation of mucinous material within the peritoneal cavity, most commonly originating from appendiceal mucinous neoplasms. We report a case of PMP secondary to appendiceal mucocoele, emphasizing its imaging characteristics, surgical management, and postoperative outcome. A 62-year-old man presented with a six-month history of progressive abdominal pain and distension. Laboratory tests revealed elevated inflammatory markers and increased CA 19-9 level. Ultrasonography (US) demonstrated diffuse microcystic lesions and cystic dilatation of the appendix consistent with appendiceal mucocoele. Contrast-enhanced computed tomography (CT) showed widespread low-attenuation mucinous ascites with characteristic hepatic scalloping and peritoneal involvement. The patient underwent cytoreductive surgery (CRS) including right hemicolectomy, peritonectomy, splenectomy, and cholecystectomy. Histopathological examination confirmed high-grade appendiceal mucinous neoplasm associated with serosal mucinous adenocarcinoma. Postoperative follow-up imaging at one year demonstrated regression of intra-abdominal mucinous collections. This case highlights the importance of imaging in the early diagnosis, staging, and surgical planning of PMP. Recognition of characteristic radiological findings is essential for timely management and improved clinical outcomes.

Keywords: Pseudomyxoma peritonei, mucocoele, appendix

INTRODUCTION

Pseudomyxoma peritonei (PMP) is a rare clinical condition characterized by progressive intraperitoneal accumulation of mucinous material, most commonly originating from appendiceal mucinous neoplasms. Its estimated incidence is approximately 1-2 cases per million population annually, making it an uncommon but clinically significant disease.^{1,3} Patients typically present with non-specific symptoms such as abdominal pain and progressive abdominal distension, frequently resulting in delayed diagnosis.² Prognosis largely depends on histopathological grade, extent of peritoneal dissemination, and the completeness of surgical cytoreduction.⁴ This report aims to present the characteristic radiological findings of PMP secondary to appendiceal mucocoele and emphasize the importance of imaging in early diagnosis and appropriate surgical planning.

CASE

A 62-year-old male patient presented with diffuse abdominal pain persisting for six months, accompanied by progressive abdominal distension and bloating. Physical examination

revealed abdominal distension without guarding or rebound tenderness, prompting further evaluation with abdominal ultrasonography (US) and computed tomography (CT). Laboratory investigations demonstrated elevated inflammatory markers, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Serum tumor marker analysis revealed an elevated carbohydrate antigen 19-9 (CA 19-9) level of 200 U/ml.

US demonstrated widespread micro-hypoechoic cystic lesions, hepatic surface indentations caused by these lesions, and cystic dilatation of the appendix compatible with appendiceal mucocoele. Contrast-enhanced abdominal CT revealed diffuse low-attenuation mucinous intra-abdominal collections causing scalloping along the hepatic contours (**Figure 1**), together with findings consistent with appendiceal mucocoele (**Figure 2A, 2B**).

The patient subsequently underwent cytoreductive surgery, including right hemicolectomy, peritonectomy, splenectomy, and cholecystectomy. Histopathological examination confirmed high-grade appendiceal mucinous neoplasm



associated with serosal mucinous adenocarcinoma. Follow-up imaging performed one year postoperatively demonstrated regression of intra-abdominal mucinous collections (**Figure 3**).

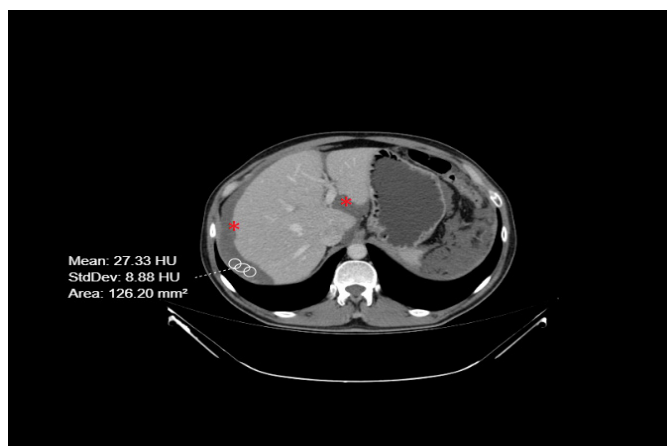


Figure 1. Axial contrast-enhanced abdominal CT image demonstrating low-attenuation mucinous perihepatic collections causing characteristic scalloping and indentations along the hepatic surface (red star markers)
CT: Computed tomography



Figure 2A. Coronal contrast-enhanced abdominal CT image demonstrating diffuse low-attenuation mucinous intra-abdominal collections distributed throughout the peritoneal cavity
CT: Computed tomography

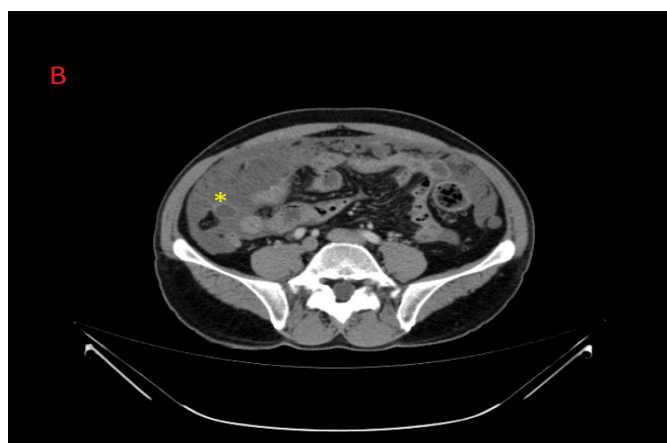


Figure 2B. Axial contrast-enhanced abdominal CT image showing cystic dilatation of the appendix (yellow star marker), compatible with appendiceal mucocoele
CT: Computed tomography

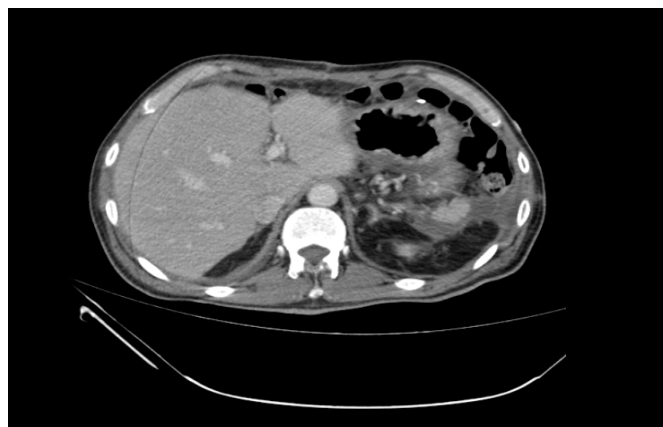


Figure 3. Axial postoperative follow-up abdominal CT image obtained one year after surgery, demonstrating marked regression of intra-abdominal mucinous collections compared with preoperative imaging
CT: Computed tomography

DISCUSSION

PMP most commonly originates from appendiceal mucinous neoplasms that disseminate into the peritoneal cavity. The disease progresses through implantation of mucin-secreting tumor cells onto peritoneal surfaces, leading to continuous mucin production and progressive accumulation within the abdomen. Over time, this process may cause gastrointestinal dysfunction, malnutrition, and significant deterioration in quality of life.⁵

Radiological imaging plays a central role in the diagnosis and management of PMP. US may demonstrate echogenic or septated intra-abdominal fluid collections, whereas CT is considered the imaging modality of choice for evaluating disease extent and preoperative staging. Typical CT findings include mucinous ascites, peritoneal thickening, hepatic scalloping, and the characteristic “omental cake” appearance, all of which strongly support the diagnosis.⁶

The differential diagnosis of PMP includes peritoneal carcinomatosis, tuberculous peritonitis, peritoneal mesothelioma, and mucinous ovarian tumors. Current treatment strategies primarily involve cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC), which has significantly improved long-term survival in selected patients. Prognosis is largely determined by histopathological grade, extent of peritoneal dissemination, and completeness of cytoreduction.^{6,7}

CONCLUSION

This case demonstrates the characteristic clinical and radiological findings of PMP. Early recognition of imaging findings is essential for timely diagnosis, accurate disease staging, and appropriate surgical planning. Prompt diagnosis and treatment may improve patient prognosis, reduce recurrence risk, and contribute to better long-term clinical outcomes.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

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Author Contributions

Concept: MFA, SY; Design: MFA, SY; Control: MFA, SY; Data Collection and/or Processing: MFA, SY; Analysis and/or Interpretation: MFA, SY; Literature Review: MFA ; Article Writing: MFA; Critical Review: MFA, SY.

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Cecal epiploic appendagitis associated with a subhepatic appendix: a case mimicking acute appendicitis

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ABSTRACT

Epiploic appendagitis is a rare, benign, and usually self-limiting inflammatory condition caused by torsion or venous thrombosis of epiploic appendages. It can clinically mimic acute appendicitis. The aim of this study is to present a case of cecal epiploic appendagitis accompanied by a subhepatically located appendix that was confused with acute appendicitis in the preoperative period, and to emphasize the diagnostic features of this rare condition. A 26-year-old male patient presented to the emergency department with right lower quadrant pain that had persisted for approximately four hours. Physical examination revealed rebound tenderness in the right lower quadrant. Laboratory findings showed leukocytosis and elevated CRP. Preoperative computed tomography (CT) demonstrated inflammatory changes within the pericecal fat and an appendix measuring approximately 5.8 mm in diameter proximally and 5 mm distally, extending into the subhepatic space. The appendix demonstrated mild wall thickening at its proximal portion. No periappendiceal fluid collection or appendicolith was observed. Although the antimesenteric location of the lesion and the pericecal dirty appearance were suggestive of epiploic appendagitis, the atypical localization and positive rebound tenderness precluded a definitive differential diagnosis. Due to persistent clinical findings and radiological uncertainty, surgical intervention was performed. Intraoperative evaluation revealed a macroscopically normal appendix; however, inflamed epiploic appendages were identified adjacent to the cecum. Appendectomy was performed along with resection of the inflamed epiploic appendages. Histopathological examination confirmed the diagnosis of cecal epiploic appendagitis with no acute inflammation detected in the appendix. Cecal epiploic appendagitis may mimic acute appendicitis in the presence of an atypical appendix location, leading to diagnostic difficulty. In such cases, surgical exploration may be necessary for definitive diagnosis and treatment of accompanying inflammatory pathology.

Keywords: Acute epiploic appendagitis, acute appendicitis, imaging, abdominal pain

INTRODUCTION

Epiploic appendages are pedunculated fatty tissue projections attached to the serosal surface of the colon. They can be found from the sigmoid colon to the cecum, running along the taenia libera and taenia omentalis. Approximately 50-100 epiploic appendages are distributed along the colon. These structures range from 0.5 to 5 cm in length, are covered by serosa, and are typically supplied by one or two arteries with a single draining vein.^{1,2}

Epiploic appendagitis is among the rare causes of acute abdominal pain and is more commonly observed in male individuals in the fourth to fifth decades of life. Its annual incidence is reported to be approximately 8.8 per 1.000.000. The incidence is higher in obese individuals.^{3,4}

Primary epiploic appendagitis is a rare, benign, and usually self-limiting inflammatory condition resulting from torsion, venous thrombosis, or ischemia of the appendages. It most commonly occurs at the sigmoid colon level, with cecal involvement being rarer.⁵

The differential diagnosis between secondary epiploic appendagitis (SEA) and primary etiologies must be clearly established. SEA refers to inflammation resulting from the spread of adjacent inflammatory processes such as diverticulitis or cholecystitis to the epiploic appendages; diverticulitis is the most common source of inflammation in this context.⁶



Cecal epiploic appendagitis may cause diagnostic difficulties due to its ability to mimic other acute abdominal pathologies such as acute appendicitis or diverticulitis.⁵

The possibility of confusion with acute appendicitis in patients presenting with right lower quadrant pain underscores the importance of imaging modalities for accurate diagnosis.⁷ Today, preoperative diagnosis can most often be established by computed tomography (CT). Typical CT findings include periappendiceal fat stranding, increased appendiceal diameter, and an oval mass with peripheral hyperdensity in an antimesenteric location, reflecting inflammatory fat and sometimes a thrombosed vessel.^{8,9}

Although epiploic appendagitis is generally managed conservatively, conditions requiring surgery—such as acute appendicitis—cannot always be excluded in the presence of atypical clinical and radiological findings. In such situations, surgical exploration may be required due to diagnostic uncertainty.¹⁰

The subhepatic location of the cecum and appendix is an uncommon anatomical variant that may result from either intestinal malrotation or incomplete descent of the cecum during embryological development. Intestinal malrotation occurs because of incomplete or absent rotation of the primitive midgut around the superior mesenteric artery between the 5th and 10th weeks of fetal life, followed by abnormal fixation to the peritoneal wall. Alternatively, a subhepatic cecum may arise when the cecum fails to descend to the right iliac fossa despite otherwise normal intestinal rotation. The position of the appendix is highly variable; while the retrocecal location is the most common, followed by pelvic, subcecal, preileal, and postileal positions, atypical locations such as subhepatic, left-sided, intrahernial, mesocolic, and lumbar positions have also been described. Awareness of these anatomical variations is clinically important, as unusual appendiceal locations may alter the presentation of right lower quadrant pathologies, mimic other intra-abdominal diseases, and lead to diagnostic challenges and delays in management.¹¹

In this study, we present a case of cecal epiploic appendagitis associated with a subhepatically located appendix that was confused with acute appendicitis in the preoperative period and was confirmed surgically and histopathologically.

CASE

A 26-year-old male patient with no comorbidities presented to the emergency department with right lower quadrant abdominal pain that had persisted for 4 hours. The pain was localized and showed no migration. There was no history of nausea, vomiting, or fever.

Physical examination revealed tenderness in the right lower quadrant without guarding; rebound tenderness was positive. Rovsing, psoas, and obturator signs were negative.

Laboratory findings showed a leukocyte count of $11.07 \times 10^3/\mu\text{L}$ and a CRP level of 9.17 mg/dL. Other parameters were within normal limits.

Preoperative CT examination revealed marked inflammatory changes in the pericecal fat tissue (**Figure 1**). The appendix was found to extend into the subhepatic space with a proximal diameter of approximately 5.8 mm (**Figures 1, 2**). Appendiceal wall thickening or luminal obstruction was not clearly identified. However, acute appendicitis could not be excluded given the existing inflammatory changes, the unusually long course of the appendix, and its atypical localization.

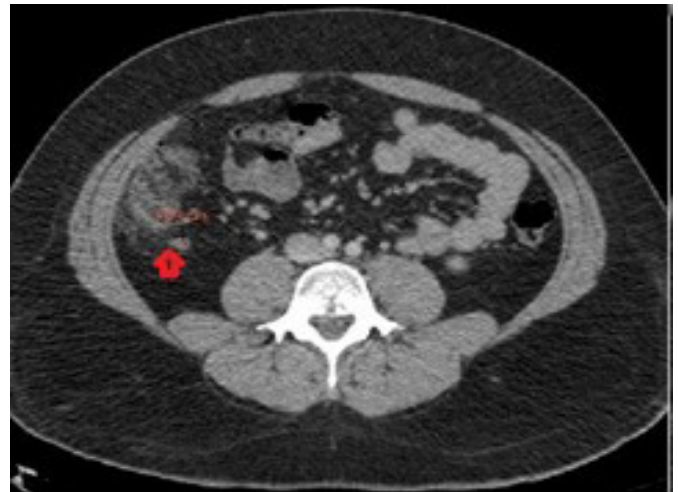


Figure 1. Pericecal dirty appearance and the appendix indicated by an arrowhead



Figure 2. Extension of the appendix into the subhepatic space

In view of persistent clinical findings and inconclusive radiological results, the patient was taken to the operating room. Intraoperative examination revealed that the appendix was in a subhepatic location and appeared macroscopically normal (**Figure 3**). However, multiple inflamed epiploic appendages were identified adjacent to the cecum (**Figure 4**). Appendectomy and resection of the inflamed epiploic appendages were performed.

Intraoperative and histopathological examination revealed no evidence of acute inflammation in the appendix. Histopathological evaluation confirmed the diagnosis of epiploic appendagitis. The postoperative course was uneventful, and the patient was discharged in good clinical condition.

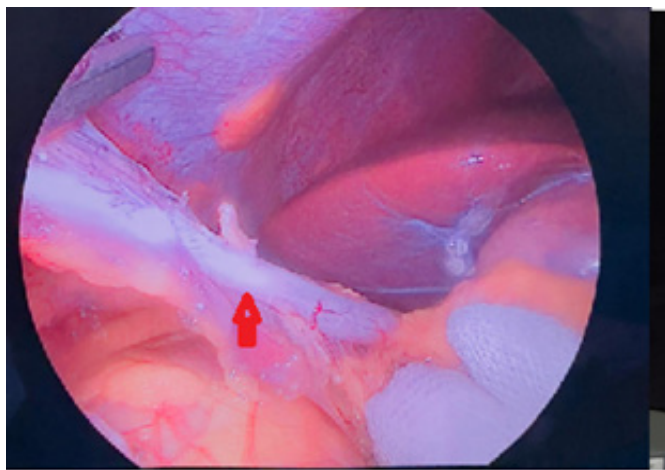


Figure 3. Normal appendix appearance

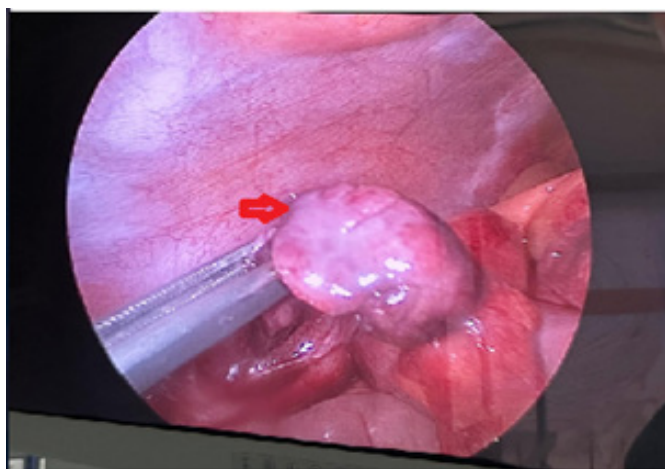


Figure 4. Inflamed cecal epiploic appendages

DISCUSSION

Epiploic appendagitis is a rare and frequently underrecognized cause of acute abdominal pain. Misdiagnosis may lead to unnecessary hospitalization, antibiotic use, or surgical intervention. Although advances in imaging have improved recognition of this condition, clinical awareness remains of critical importance.¹²

Epiploic appendagitis most commonly occurs at the sigmoid colon level and less frequently involves the descending colon and cecum.¹ Reaching a definitive diagnosis may be challenging, particularly in the presence of atypical anatomical variations such as a subhepatically located appendix.¹³ CT remains an important imaging tool for resolving diagnostic complexity and preventing unnecessary surgery in this setting.⁸

However, the intraoperative discovery of epiploic appendagitis in patients with a preliminary diagnosis of acute appendicitis or diverticulitis may complicate surgical decision-making.¹⁴ Surgical excision may be considered especially in cases that do not respond to conservative treatment or in which symptoms recur. Furthermore, the presence of anatomical variations such as a subhepatic appendix may further complicate the clinical picture and necessitate resection of additional pathologies.¹⁵

Although conservative management of epiploic appendagitis is increasingly accepted,^{11,16} prospective studies on the indications and timing of surgical intervention in specific cases remain insufficient. The lack of randomized controlled trials evaluating the efficacy of conservative treatment in patients diagnosed with EA (epiploic appendagitis) makes it difficult to standardize a uniform treatment approach.¹⁷

In the present case, the decision to proceed with surgery was mainly driven by diagnostic uncertainty rather than by epiploic appendagitis itself. Although CT findings were suggestive of cecal epiploic appendagitis, acute appendicitis could not be confidently excluded because of the subhepatic location of the appendix, mild wall thickening at its proximal portion, right lower quadrant tenderness, leukocytosis, and elevated CRP levels. Therefore, conservative management was considered less reliable in this atypical setting. Surgical exploration was performed to avoid missing a possible acute appendicitis in an unusual anatomical location and to establish a definitive diagnosis. This case highlights that the coexistence of cecal epiploic appendagitis and a subhepatic appendix may create a diagnostic gray zone in which radiological findings, although suggestive, should be interpreted together with clinical and laboratory findings.

The literature on imaging findings of inflammatory processes associated with a subhepatically located appendix is limited.¹³ Therefore, as in our case, intraoperative evaluation and histopathological confirmation play a critical role in establishing an accurate diagnosis and determining the appropriate treatment strategy in cases with atypical presentations.¹⁸

CONCLUSION

Epiploic appendagitis is a rare condition that may be confused with acute appendicitis, particularly in patients presenting with right lower quadrant pain. In the presented case, acute appendicitis could not be safely excluded due to the subhepatic localization of the appendix and accompanying pericecal inflammatory changes; therefore, surgical exploration was preferred. Intraoperative and histopathological evaluation revealed no inflammation in the appendix; however, the inflamed epiploic appendages adjacent to the cecum were resected, confirming the diagnosis.

This case demonstrates that epiploic appendagitis may create significant diagnostic complexity in the presence of atypical anatomical variations and that a surgical approach may be inevitable in some situations. Therefore, the combined and careful evaluation of clinical and CT findings is of paramount importance.

ETHICAL DECLARATIONS

Informed Consent

Written informed consent was obtained from the patient included in this report. Signed consent forms are retained by the authors and are available upon request.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

This case report did not receive any financial support.

Author Contributions

Concept: NI, IO; Design: NI, IO; Data Collection and/or Processing: NI; Analysis and/or Interpretation: NI, IO; Literature Review: NI; Article Writing: NI; Critical Review: NI, IO.

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