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Rôle de l'IRM et des séquences cinétiques dans le bilan préopératoire des tumeurs de l'oesophage

Haefliger Laura

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Faculté de biologie
et de médecine

UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Département de Radiologie
Service de radiologie diagnostique et interventionnelle

**Rôle de l'IRM et des séquences cinétiques dans le bilan
préopératoire des tumeurs de l'œsophage**

THESE

préparée sous la direction du Professeur Clarisse Dromain

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

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2023

IMPRIMATUR

La Faculté de biologie et médecine de l'Université de Lausanne, sur proposition du jury, autorise l'impression de la thèse de doctorat rédigée par

Laura Denise HAEFLIGER

intitulée

*Rôle de l'IRM et des séquences cinétiques dans
le bilan préopératoire des tumeurs de l'œsophage*

sans se prononcer sur les opinions exprimées dans cette thèse.

Directrice	Professeure Clarisse Dromain
Expert interne	Docteur Rafael Duran
Vice-directeur de l'Ecole doctorale	Professeur John Prior

Lausanne, le 10.10.2023



pour Le Doyen
de la Faculté de Biologie et de Médecine

Monsieur le Professeur John Prior
Vice-Directeur de l'Ecole doctorale

RÉSUMÉ

Article **“Esophageal cancer T-staging on MRI: A preliminary study using cine and static MR sequences”**

Le cancer de l'œsophage est le 6^{ème} cancer le plus fréquent à travers le monde. Son traitement est décidé en fonction de son stade initial selon la classification TNM. La stadification locale de la tumeur nommée « T-staging » est très importante surtout pour les patients qui pourraient bénéficier d'une chirurgie.

Actuellement l'écho-endoscopie (EUS) et le CT scanner sont les examens de choix pour l'évaluation du stade loco-régional de la tumeur. L'IRM est néanmoins de plus en plus utilisée grâce à sa meilleure résolution tissulaire, sa technique moins invasive que l'EUS, et ses résultats plus complets lors de sténose œsophagienne sévère (le passage de l'endoscope pouvant être limité). Il est également possible d'utiliser des séquences IRM cinétiques afin d'étudier la mobilité et la motilité intrinsèque des organes, comme lors d'examen cardiaque. Dans le système digestif supérieur, ces séquences ont été étudiées principalement pour les anomalies du péristaltisme œsophagien.

Dans notre étude, nous avons utilisé les séquences cinétiques pour étudier le mouvement de la tumeur par rapport aux organes adjacents (le cœur, la trachée et les bronches, la plèvre, l'aorte et le diaphragme). Les anomalies de la mobilité entre la tumeur et les structures adjacentes sont un indicateur de l'infiltration tumorale des structures.

En évaluant dans un premier temps les séquences statiques puis en ajoutant à l'analyse les séquences cinétiques, nous avons montré dans ce travail que l'imagerie de la tumeur œsophagienne par l'IRM permet un T-staging fiable. L'ajout des séquences cinétiques est une plus-value, et permet une meilleure distinction entre les tumeurs de stade avancé, avec une confiance diagnostique accrue et une meilleure concordance entre les radiologues sur le stade tumoral.

Rôle Laura Haefliger MD

Pour ma thèse MD j'ai effectué tout le prélèvement des données démographiques des patients en m'occupant du CRF de l'étude STIRMCO dans laquelle les patients étaient inclus, ainsi que de l'analyse des résultats d'imagerie des différents examens de chacun des patients. J'ai organisé et participé à l'analyse des images en tant que co-lectrice pour les résultats. J'ai écrit l'introduction, une partie des matériel et méthode et des résultats, et la discussion de l'article et est géré la bibliographie. J'ai également créé les figures illustratives et les tableaux. Par la suite je me suis occupée de la soumission de l'article et des corrections demandées selon commentaires des reviews.

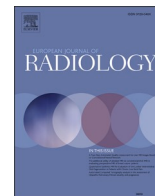
J'ai présenté oralement mon papier au congrès européen d'imagerie digestive ESGAR en 2022 à Lisbonne.

Mon co-auteur Dr Mario Jreige a participé en s'occupant des analyses statistiques de l'étude et a co-écrit les matériel et méthodes et résultats. Il a produit les figures statistiques. Il a apporté des modifications et corrections au manuscrit et a participé à la soumission.

Veuillez recevoir mes meilleures salutations

Laura Haefliger

A handwritten signature in black ink, appearing to read 'Haefliger', written in a cursive style.



Esophageal cancer T-staging on MRI: A preliminary study using cine and static MR sequences

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ABSTRACT

Objectives: To evaluate the added value of cine MR in addition to static MRI for T-Staging assessment of esophageal cancer (EC).

Materials and methods: This prospective monocentric study included 54 patients (mean age 66.3 ± 9.4 years, 46 men) with histologically proven EC. They underwent MRI on a 3 T-scanner in addition to the standard workup. Acquisitions included static and cine sequences (steady-state-free-precession and real-time True-FISP during water ingestion). Three radiologists independently assessed T-staging and diagnosis confidence by reviewing (1) static sequences (S-MRI) and (2) adding cine sequences (SC-MRI). Inter-reader agreement was performed. MRI T-staging was correlated to reference standard T-staging (histopathology or consensus on endoscopic ultrasonography and imaging findings) and to clinical outcome by log-rank test.

Results: Both S-MRI and SC-MRI T-staging showed a significant correlation with reference T-staging ($r_s = 0.667$, $P < 0.001$). SC-MRI showed a slightly better performance in distinguishing T1-T3 from T4 with a sensitivity, specificity and AUC of 76.5% (95% CI: 50.1–93.2), 83.8% (68–93.8) and 0.801 (0.681–0.921) vs 70.6% (44–89.7), 83% (68–93.8) and 0.772 (0.645–0.899) for S-MRI. Compared to S-MRI, SC-MRI increased inter-reader agreement for T4a and T4b ($\kappa = 0.403$ and 0.498) and T-staging confidence.

Conclusion: MRI is accurate for T-staging of EC. The addition of cine sequences allows better differentiation between T1-T3 and T4 tumors with increased diagnostic confidence and inter-reader agreement.

1. Introduction

Treatment and survival of locally advanced esophageal cancer (EC) has evolved in the last decades thanks to the implementation of neoadjuvant and adjuvant therapy [1,2]. Surgery is still the fundament of curative treatment for locally advanced resectable EC but remains associated with a high morbidity [1]. Definitive chemoradiotherapy (CRT) with surveillance or salvage esophagectomy for local tumor control is also a recommended option [3]. Accuracy of depth of invasion of EC (T-Staging) for selection of patients who can benefit from neoadjuvant therapy and surgery or definitive CRT is therefore crucial.

Initial clinical staging of EC is based on the TNM classification (8th edition from American Joint Committee on Cancer) [4,5] using endoscopic ultrasound (EUS), contrast-enhanced-computed-tomography (CE-CT) and ¹⁸F-fluorodeoxyglucose-positron-emission-tomography with computed-tomography (¹⁸FDG-PET-CT) [3]. TNM classification is important to perform a prognostic stage group [5].

EUS is currently the method of reference to determine esophageal wall tumoral extension, with a performance index of 0.89 for esophageal cancer [6] and a T-staging accuracy ranging between 60 and 97% [7,8]. However, this method can be limited in locally advanced and stenotic tumor [6]. MRI has a high contrast resolution, and has the potential to be

Abbreviations: EC, Esophageal cancer; CRT, chemo-radiotherapy; EUS, Endoscopic ultrasonography; CE-CT, Contrast enhanced computed tomography; SSFP, Steady state free precession; True-FISP, True fast imaging steady-state precession; DB, Dark Blood; TSE, Turbo spin echo; ADC, Apparent Diffusion Coefficient; DWI, Diffusion Weighted Imaging; S-MRI, Static MRI; SC-MRI, Static + Cine MRI; ROC, Receiver operating characteristic.

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more accurate, less invasive and more reproducible than EUS [9–12]. It has an overall good sensitivity (92%) in detecting EC [13]. The American College of radiology currently recommends it as a “may be appropriate” imaging technique for EC staging [14]. MRI also offers the possibility of combining analysis of morphological features and kinetic information, with more precision on relation of EC with surrounding structures.

Due to intrinsic peristalsis of esophagus and surrounding mediastinal structures, MRI can be technically challenging due to kinetic artefacts. The idea to use this intrinsic peristalsis to analyze structures has been initially developed for cardiac MRI, with development of kinetic Real-time sequences [15,16]. Similar technical approaches were investigated for esophagus and gastric diseases, especially for the assessment of esophageal motility disorders [10,17–19], gastro-esophageal reflux [20,21] and hiatal hernias [22]. Currently, only a limited number of studies have investigated the potential value of cine MRI for EC detection or delineation [23,24], quantification of EC motion [24] and staging [25]. Only one group studied the effect of EC on esophageal peristalsis: *Koyama et al.* used a steady state free precession (SSFP) cine sequence on EC and showed that partial or complete interruption of peristalsis was associated with locally advanced T3-T4 tumors [25].

In this study, we used the hypothesis that when disease is locally invasive, peristalsis and mobility of EC with the surrounding structures will be impaired, allowing a better accuracy in the local evaluation of the tumor. We therefore used addition of cine MR to static MR to evaluate the performance of MRI for T-staging, and its prognostic significance.

2. Material and methods

2.1. Study design

This is a prospective, single-institution, institutional review board-approved study (ID CER-VD 2017-00388; NCT03347630). Patients were addressed after selection by our oncologist and digestive surgeons between October 2017 and December 2021. Written informed consent was obtained for all participants prior to study inclusion. Inclusion criteria were adult patients with newly pathologically proven EC of any histological type, including gastro-esophageal junction cancers. Exclusion criteria were (1) patients with MRI contraindications, (2) patients with cervical EC (for whom surgery is not indicated) and (3) patients already treated for EC. Each patient underwent MRI examination in addition to the standard initial workup including EUS, CE-CT and ^{18}F -FDG PET-CT within 2 weeks prior initiation of treatment. Final population included 54 patients (Fig. 1). Demographic, clinical, histopathological data and outcomes were collected from electronic medical records.

2.2. MRI acquisitions

MRI were acquired on a 3 T-scanner (Magnetom PrismaFit, Siemens Healthcare) with two 16-channel body array coil and a 32-channel spine coil (Siemens Healthcare). Static MRI sequences included (1) T2 weighted imaging (wi) Blade in sagittal and axial planes covering thorax and whole liver, (2) gated T2wi turbo spin echo (TSE) dark-blood (DB) centered on the tumor in a perpendicular plane, (3) axial diffusion weighted imaging (DWI) (b50, 400, 800 s/mm²) and ADC map covering the thorax and whole liver (4) T1wi Volume Interpolated breathhold examination (VIBE) Dixon in axial plane before and after injection of Gadolinium (Dotarem® 0.5 mmol Gd/ ml, Guerbet, Roissy, France), at the arterial, venous and late phases (supplementary table 1, supplementary Fig. 2A-D).

Cine MRI sequences included (1) steady state free precession (SSFP) in sagittal and perpendicular plans relative to the tumor and (2) one transverse slice real-time cine True fast imaging steady-state precession (True-FISP) during water ingestion, centered on the tumor (supplementary table 2 and supplementary Fig. 2E-G, supplementary material movie 1 to 3).

The median acquisition time was 62 min (range: 42–89 min). The static sequences acquisition lasted approximately 45 min while the kinetic sequences acquisition lasted around 15 min. Acquisition time variability is attributed to patients’ breathing variation and tumor size.

2.3. Image analysis

Three radiologists (__,_ and_) with 25, 10 and 2 years of expertise in abdominal radiology, respectively) independently reviewed the MR examinations. Readers were aware of the present study goal but blinded to all clinical data and results of other imaging modalities. Two sets of reading were analyzed during the same reading session on a picture archiving and communication system (PACS):

- Set 1 (S-MRI): Static sequences including T2wi Blade, T2wi TSE DB, DWI and corresponding ADC map, and T1wi VIBE with dynamic sequences.
- Set 2 (SC-MRI): S-MRI with addition of cine sequences including sagittal and transverse SSFP images targeted on the tumor volume.

Readers were asked to analyze set 1 and complete the T-staging according to the 8th edition of UICC-AJCC TNM classification [4] (supplementary table 3). All the different injection phases were used for T-staging assessment without separate analysis. Due to a lack of performance by distinguishing invasion of submucosa from muscularis propria on MRI, T1 and T2 stages were grouped [12,26].

Readers then assessed set 2 and completed a second T-staging evaluation. On cine MR, invasion of adjacent organ by the tumor was

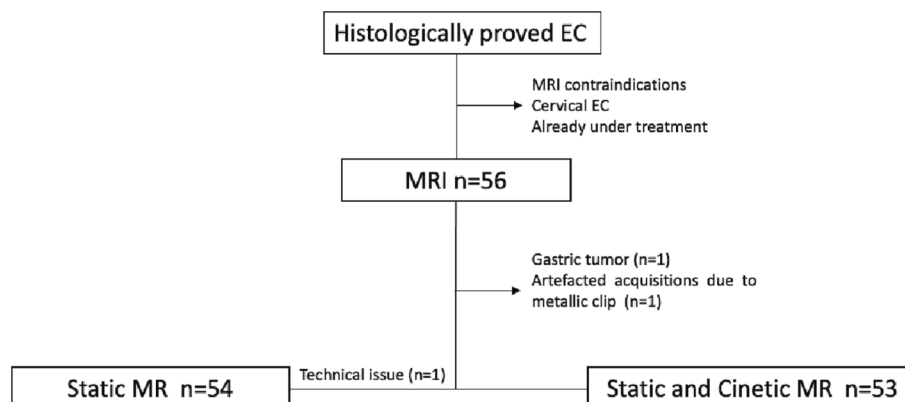


Fig. 1. Flowchart of the study. Abbreviations: EC: Esophageal cancer.

suspected in case of close contact between the tumor and the organ with a loss of fat planes or a mass effect, in addition to disruption of mobility between the two structures (Fig. 2 and Fig. 3, supplementary Fig. 4, supplementary material movie 1 to 3).

Consensus was finally performed by the 2 expert readers in all discordant cases for statistical purposes. In addition to the T-staging evaluation, the readers were asked to assess their confidence for each reading set using a 3-points scale: high, intermediate or low confidence.

The following tumor parameters were assessed: tumor location and length, presence of upstream esophagus dilatation, mean and minimal ADC values of tumors > 10 mm of maximal diameter. On cine True-FISP images, maximal tumor thickness and the maximum and minimal opening diameter of the esophagus were measured at the tumor level during water ingestion (supplementary Fig. 3, supplementary material movie 4 and 5). Tumors were considered as responsible for stenosis when the minimal lumen opening diameter during water ingestion was < 10 mm.

2.4. Reference standard

The reference standard for T-staging was based on histo-pathological analysis of the tumor specimen for patients undergoing upfront surgery, and on the consensus based on all endoscopic and imaging findings for the others. As the majority of patients had neoadjuvant treatment before surgery (53.7%) or non-surgical treatment (35.1%) (Table 1), a direct correlation with pathology result was not always possible. We used as the reference staging the consensus performed during the interdisciplinary tumor board between endoscopic and standard imaging protocols according to ESMO recommendation including EUS and CE-CT for loco-regional staging and ¹⁸F-FDG PET/CT for loco-regional and distant staging [3]. Four patients had a complementary bronchoscopy when bronchial invasion was suspected (supplementary table 4).

2.5. Statistical analysis

Demographic and clinical characteristics were analyzed by producing tables of frequency for categorical variables and calculating the median and 95% confidence interval (CI) or mean and standard deviation (SD) for continuous variables.

The correlation of T-staging between MRI and reference standard was determined using Spearman's correlation. Receiver operating characteristics (ROC) curves, sensitivity and specificity of S-MRI and SC-

MRI in determining the T-stage were calculated. Logistic regressions were used to determine the best-fitting model for predicting T-stage between S-MRI and SC-MRI.

Inter-reader agreement was calculated for readers consensus between S- and SC-MRI using Cohen's kappa coefficient (κ). Kappa values < 0.40 were considered poor agreement; 0.41–0.75 were considered moderate to good agreement; and over 0.75 were considered excellent agreement. Comparison between cine and static MRI findings was performed using Pearson's, Chi2 test or Spearman correlation, as appropriate.

All statistical analyses were performed using STATA version 14.2 (STATA Corp., Texas, USA). *P* values < 0.05 were considered as statistically significant.

3. Results

3.1. Study population

Among the 54 included patients, 46 were men (85%), with mean age of 66.3 ± 9.4 years. Patients and tumor characteristics are summarized in Table 1. Thirty patients (55.6%) had adenocarcinoma, 22 (40.7%) had squamous cell carcinoma, and 2 (3.7%) had neuroendocrine carcinomas. Fifty-three patients completed static and cine MR (Fig. 1).

Tumor location based on MRI was in the upper third (*n* = 2, 3.7%), middle third (*n* = 13, 24.1%), lower third (*n* = 15, 27.8%) of the esophagus and at the gastro-esophageal junction (*n* = 24, 44.4%). Among the latter, 8 were classified Siewert I (33.3%), 12 Siewert II (50%) and 4 Siewert III (16.7%). Twelve patients (22.2%) were asymptomatic, 8 (14.8%) had complete dysphagia and 34 (62.9%) had partial dysphagia. Thirty-five patients (64.8%) were treated with surgery including 6 (11.1%) with upfront surgery and 29 (53.7%) after neoadjuvant treatment.

The median follow-up was 23.6 months (95% CI: 15–32.1 months, range: 1.8–47.7 months). Two patients (*n* = 3.7%) died prematurely during follow-up, one due to cardiac arrest and the second one due to EC-related surgical complication. Outcome of the 52 remaining patients included 29 (53.7%) in remission, 8 (14.8%) with loco-regional recurrence, 10 (18.5%) with metastatic progression and 5 (9.2%) with stable partial response to systemic or locoregional treatment (Supplementary Fig. 1). Follow-up of patients was conducted by clinicians, based on symptoms, endoscopy and CE-CT or ¹⁸F-FDG PET-CT according to ESMO recommendations [3].

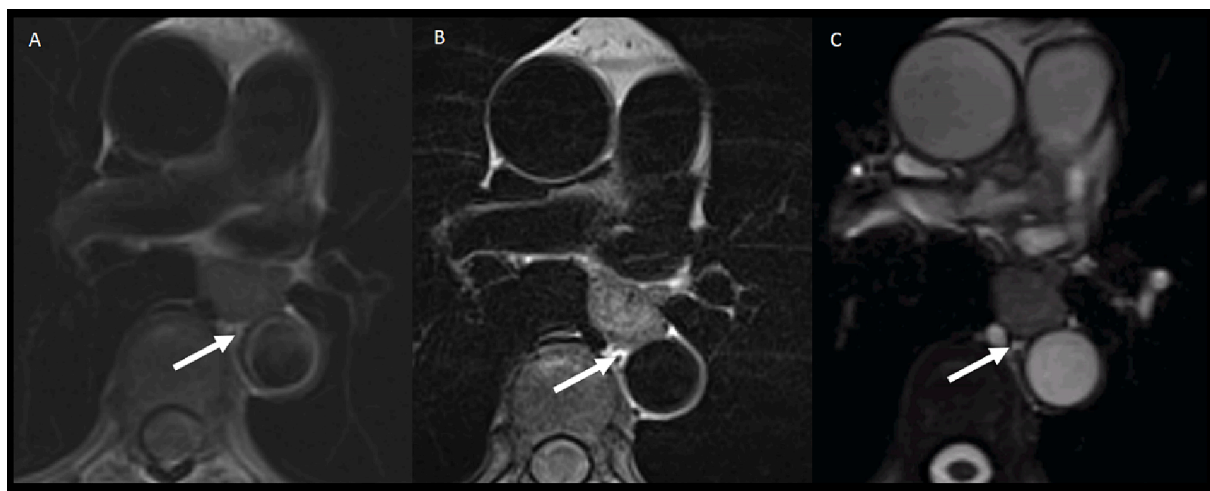


Fig. 2. 69 y.o. woman with squamous cell carcinoma of the middle third of the esophagus. On static sequences with T2wi Blade (A) and T2wi Time spine echo Dark blood (B) there is a close contact of the tumor and the aortic wall. On cine sequences SSFP (C) one timepoint (complete video available on web supplementary data Movie 5), the tumor and aortic wall have conserved mobility between each other, with dark line delineation, compatible with a T3 lesion, like the reference standard staging. Abbreviations: wi: weighted imaging TSE: time spin echo; DB: Dark Blood; SSFP: steady state free precession.

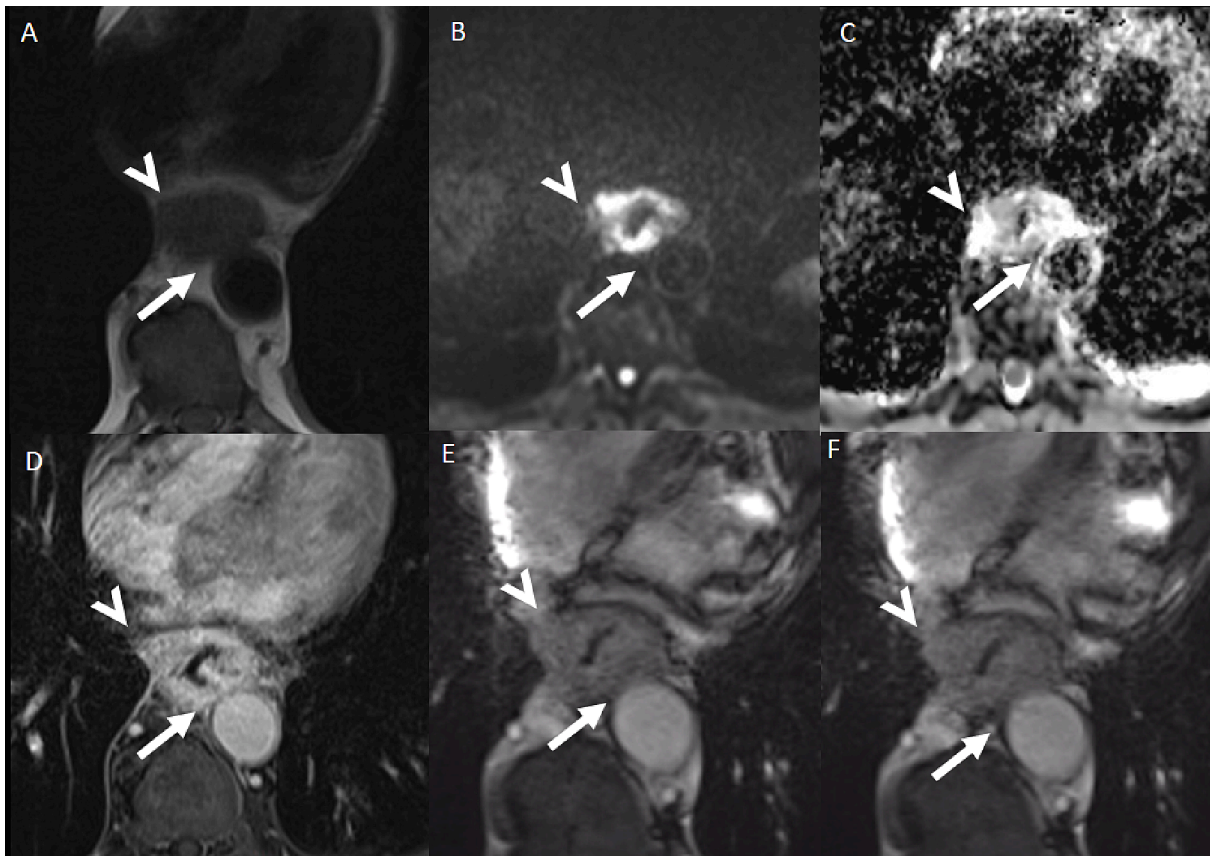


Fig. 3. 70 y.o. men with adenocarcinoma of middle third of the esophagus. On static sequences with T2-wi Blade (A), DWI and corresponding ADC map (B and C), T1-wi VIBE Dixon at 90 s after contrast injection (D), there is a close contact between the esophagus lesion and aortic wall (arrows) as well as the right pleura (arrowheads). On cine sequences (E and F, transverse SSFP two timepoints - complete video on web supplementary data [Movie 6](#)), the lesion and the aortic wall have a close contact, without mobility between each other, compatible with a T4b lesion, like the reference standard staging. Abbreviations: wi: weighted imaging; VIBE DWI: Diffusion weighted imaging; ADC: Apparent diffusion coefficient; SSFP: steady state free precession.

3.2. Imaging tumors characteristics

Evaluation of S-MRI T-staging after consensus concluded to 7 T1-T2 lesions (13.2%), 28 T3 lesions (52.8%) and 18 T4 lesions (33.9%). With the addition of cine MR sequences, one lesion was upgraded from T3 to T4 ([Table 2](#)). Details of the description of EC and eventual invasion of surrounding structures is described in [supplementary table 5](#).

Cine True-FISP sequence was acquired in 37/53 (69.8%) patients without severe dysphagia nor swallowing disorder but considered of enough quality in 31 patients. Twenty-six tumors (70.2%) were classified as stenotic. The mean maximal tumor wall thickness was 16.4 ± 7.6 mm and was significantly higher in tumors with stenosis (19.9 ± 10.3 mm) compared to non-stenotic tumor (2.6 ± 1.5 mm) ($p < 0.0001$) and significantly higher in T3-T4 (20.8 ± 10.9 mm) compared to T1-T2 (6 ± 2.9 mm) ($p = 0.0002$). A statistically significant difference was found in the rate of tumor stenosis depending to the T-stage, with 92.3% of patient with stenosis in T3-T4 versus 20% in T2 ($p < 0.001$).

The median tumor length was 56.5 mm (range: 13–120 mm). Twenty-one patients (39%) had upstream esophageal dilatation.

Mean and min ADC mean values, measured in 50/54 patients, were 1466 ± 306 and $1114 \pm 308 \times 10^{-6} \text{ mm}^2/\text{sec}$, respectively. We found a trend for a higher ADC_{mean} in T1-T2 compared to T3-T4 (1639 versus $1421 \times 10^{-6} \text{ mm}^2/\text{sec}$, $p = 0.051$). We found a statistically significant negative correlation between ADC_{mean} and the maximal tumor wall thickness ($\rho = -0.44$, $p = 0.020$) ([Fig. 4](#)).

3.3. Comparison of S-MRI, SC-MRI, and reference standard T staging

Reference T-staging was obtained from pathological examination of the resected EC in 6 patients (11.1%) and consensus from all endoscopic and imaging procedures in 48 patients (88.9%) ([supplementary table 4](#)).

Comparison of S-MRI, SC-MRI and reference T-staging were made on 53/54 patients having both static and SSFP cine sequences ([Table 2](#)). Both S-MRI and SC-MRI T-staging showed a significant correlation with reference T staging ($r_s = 0.667$, $p < 0.001$). SC-MRI showed similar performance to S-MRI in distinguishing T1-T2 from T3-T4 with a sensitivity, specificity and AUC of 95.8% (95% CI: 88.5–99.9%), 75% (34.9–96.8%) and 0.864 (0.702–1), respectively. SC-MRI showed a slightly better performance in distinguishing T1-T3 from T4 with a sensitivity, specificity and AUC of 76.5% (50.1–93.2%), 83.8% (68–93.8%) and 0.801 (0.681–0.921), respectively for SC-MRI vs 70.6% (44–89.7%), 83% (68–93.8%) and 0.772 (0.645–0.899), respectively for S-MRI ([Table 3](#); [Fig. 5](#)) without statistical significance ($p = 0.317$, $p = 1$, $p = 0.317$, respectively).

3.4. Inter-reader agreement and staging confidence

Inter-reader agreement was excellent for T1-T2 ($\kappa = 1$ and 0.947) and moderate to good for T3 stages ($\kappa = 0.552$ and 0.530) for SC-MRI and S-MRI, respectively. For T4a and T4b-stages, inter-reader agreement was better for SC-MRI ($\kappa = 0.403$ and 0.498) than for S-MRI ($\kappa = 0.376$ and 0.122). SC-MRI showed an increase in T-staging confidence compared to S-MRI for all readers in +17% and +21% of cases ($n = 9/n = 11$) for expert readers and +24% of cases ($n = 13$) for the junior

Table 1
Demographic and tumor characteristics.

Patients N = 54	N (%)
Age years mean (range)	66.3 ± 9.4 (41–83)
Sex (Female/male)	8(15)/46(85)
Histological type n (%)	
Adenocarcinoma	30 (55.6)
Squamous cells	22 (40.7)
Neuroendocrine	2 (3.7)
Histologic Grade n (%)	
Grade 1	4 (7.4)
Grade 2	25 (46.2)
Grade 3	23 (42.5)
Grade unknown	2 (3.7)
Location (%)	
Upper third esophagus	2 (3.7)
Middle third esophagus	13 (24.1)
Lower third esophagus	15 (27.8)
Gastro-esophageal junction	24 (44.4)
Sievert I	8 (33.3)
Sievert II	12 (50)
Sievert III	4 (16.7)
Chronic alcohol consumption	
Active	25 (46.2)
Past	2 (3.7)
Absent	27 (50)
Smoking status	
Active	24 (44.4)
Past	11 (20.4)
Absent	19 (35.2)
Symptoms	
Absent	12 (22.2)
Partial dysphagia	34 (62.9)
Complete dysphagia	8 (14.8)
Clinical Stage[3]	
I	0 (0)
II	9 (16.6)
III	24 (44.4)
IVa	16 (29.6)
IVb	5 (9)
Type of treatment	
Upfront surgery	6 (11.1)
Neoadjuvant treatment	29 (53.7)
Definitive radio-chemotherapy	12 (22.2)
Palliative chemotherapy	7 (12.9)
Patient outcome	
Remission	29 (53.7)
Loco-regional recurrence	8 (14.8)
Distant metastatic progression	10 (18.5)
Stable or partial response	5 (9.2)
Premature death	2 (3.7)

Abbreviations: N: number, T: Tumor staging, EUS: Endoscopic ultrasonography.

Table 2
Comparison of T-staging between S-MRI, SC- MRI and reference standard.

	T1-T2 n (%)	T3 n (%)	T4 n (%)
S-MRI (n = 53)	7 (13.2)	28 (52.8)	18 (33.9)
SC-MRI (n = 53)	7 (13.2)	27 (50.9)	19 (35.8)
Reference standard (n = 53)	8 (15.1)	28 (52.8)	17 (32.1)

Abbreviations: S-MRI: Static MRI; SC-MRI: Static + Cine MRI.

reader considering any increase in confidence level.

4. Discussion

Our study showed a high performance of MRI for initial T-staging, particularly for high stages, with a significant correlation between MRI T-staging and reference T-staging for both S-MRI and SC-MRI. Due to the difficulty to distinguish either contact or invasion of loco-regional structures, the inter-reader agreement was lower in higher stages. The addition of cine sequences helped to improve this agreement.

The assessment of tumor location and T-staging of EC are important for disease management, treatment decision and surgery planning. To date, MRI is not routinely included in the T-staging protocols of EC but several studies have highlighted its high accuracy and sensitivity for initial staging [9,11–13,26–29]. Our results are in line with previous studies reporting the high diagnostic performance of MRI in the differentiation between early (T1-T2) and locally advanced tumor (T3-T4) [12]. A recent meta-analysis of 20 studies including 984 patients has assessed the performance of MRI in differentiating ≤ T2 vs > T3-stage for EC and has reported 86 % for both sensitivity and specificity, which is actually similar to EUS and CE-CT [8,13]. In a study of 70 patients Guo et al. [9] demonstrated an accuracy of 82% for CE-CT, 81% for EUS and 96% for MRI in stratifying patients with EC confined to the wall versus extending beyond. In the Giganti et al. study, MRI was more specific (92%) with a better accuracy (83%) than EUS (specificity 75%, accuracy 78%) and CE-CT (specificity 67%, accuracy 78%) (27).

In the present study, we evaluated the usefulness of cine MR sequences in addition to static MR sequences for the assessment of adjacent organs invasion. We tested two different types of cine MR sequences: (1) SSFP sequence to assess the mobility between the tumor and adjacent organs, (2) real-time True-FISP during water ingestion to assess the degree of tumor stenosis and the tumor wall thickness. Due to swallowing and dysphagia problems, True-FISP imaging was carried out only in 31 of the 54 patients (57.4%). As expected, the rate of esophageal stenosis analyzed using True-FISP images was positively correlated with the T-staging and with the tumor thickness. We also found a significant negative correlation between tumor thickness and the ADC values and a trend to have higher ADC values in T1-T2 tumor than in T3-T4 tumors in accordance with previous work from Giganti et al. [28].

Cine MRI with SSFP sequences was previously used to assess esophageal motility disorders and tumor motion for radiation therapy planning [10,24]. Only few studies have investigated the utility of cine sequences in EC [12,23,25]. Koyama et al. studied esophageal peristalsis with cine MRI in 13 patients with EC and dysphagia, and concluded that disruption of esophageal peristalsis may be an indication of muscle invasion in advanced EC [25]. Zhou et al. showed a linear correlation between tumor motion and tumor location [23]. On SSFP images, when the EC was moving independently from the adjacent organs, we determined an absence organ invasion. Conversely, when the structures appeared to adhere to each other with synchronous mobility, invasion (T4-stage) was suspected following the same idea reported by Koyama et al. in 2005 [25].

As expected, we found a similar performance of S-MRI and SC-MRI in distinguishing T1-T2 from T3-T4 (AUC: 0.864). There is trend to a better performance with SC-MRI in distinguishing adjacent organ invasion T4 from T1-T3 (+5% of sensibility and + 3% of accuracy), although not significant probably because of the small number of patients classified as T4 on reference standard (n = 17). The addition of cine sequences helped to improve the inter-reader agreement, which was higher for T4 stages using SC-MRI than S-MRI. SC-MRI was also associated to higher confidence in the T-staging for all readers but particularly for the junior reader (+24%). These results are in favor of the addition of cine MRI in the evaluation of local invasiveness in advanced tumor, and moreover when readers are less experienced. Local invasion versus local contact can be tricky to determine, and the addition of mobility can help. This is particularly important to determine if surgery is an option, even after

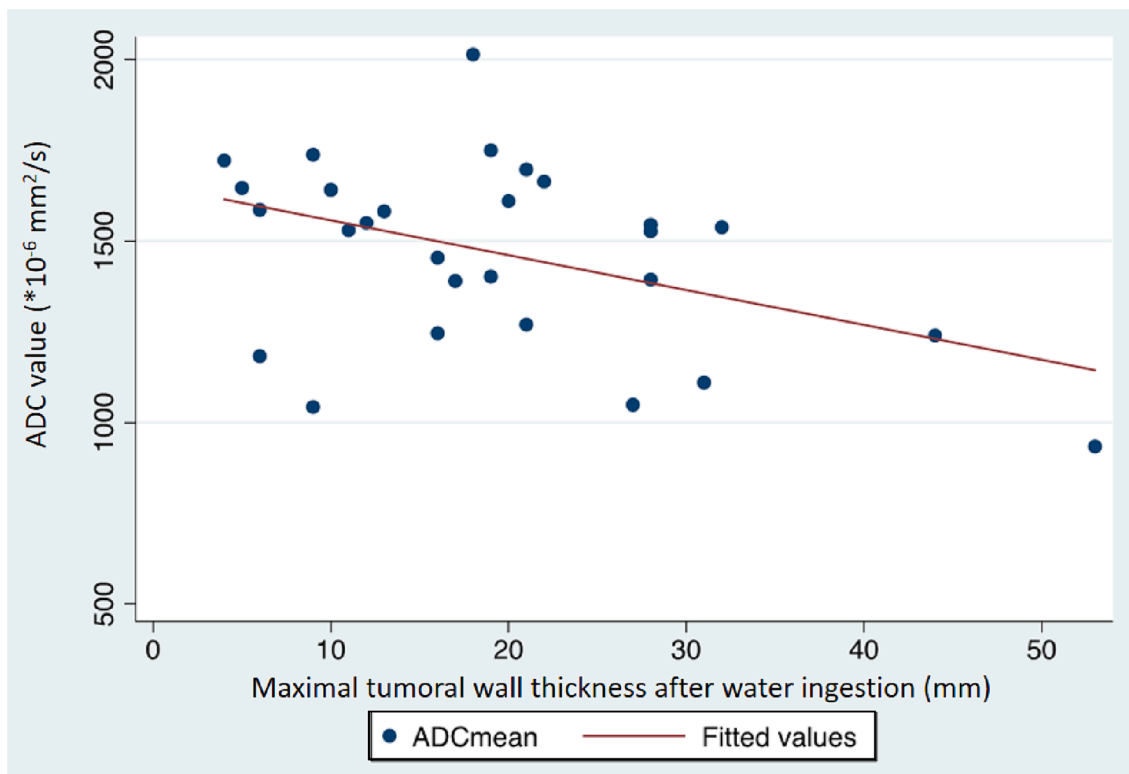


Fig. 4. Correlation between maximal tumoral wall thickness after water ingestion (mm) and ADC_{mean} values (mm²/s). *Abbreviations:* ADC: Apparent diffusion coefficient.

Table 3

Diagnostic performance of S-MRI and SC-MRI in determining the T stage, based on ROC curve analysis.

N = 53	T1-T2 vs T3-T4 (n)		T1-T3 vs T4 (n)	
	S-MRI (7 vs 46)	SC-MRI (7 vs 46)	S-MRI (35 vs 18)	SC-MRI (34 vs 19)
Sensibility	95.8%	95.8%	70.6%	76.5%
Specificity	75%	75%	83%	83.8%
AUC	0.864	0.864	0.772	0.801

Abbreviations: ROC: Receiver operating characteristic; S-MRI: Static MRI; SC-MRI: Static + Cine MRI; AUC: area under the curve.

neo-adjuvant therapy. There is also a potential value for the evaluation of the circumferential resection margins of EC. Indeed, in contrast with most of digestive organs such as colon or stomach, the esophagus has no serosal layer to limit the spread of the tumor cells and the CRM has been identified, similarly to rectal cancer, as an independent prognostic factor for recurrent disease and survival [30]. While S-MRI provides important morphological details that can help surgery planification, the cine MRI with its dynamic real-time view of the tumor and relationship with adjacent structures, could be an important parameter for identifying per and perioperative risk-assessment. It could be used to predict the potential risk of a positive surgical margin, as previously reported as present in up to 11% of esophagectomy patients [31]. Larger studies should be conducted to examine this point.

The acquisition time including morphology, functional and cine sequences in our study was around 62 min which is too long for clinical routine use. An optimized MR-protocol, based on our clinical experience and lasting around 35 min, is proposed in [supplementary material table 6](#). For this protocol, we have removed the sagittal SSFP sequence due to its lesser effectiveness in assessing the T staging and the local invasion of adjacent structures when compared to the axial SSFP sequence. The True-FISP sequence is optional and used selectively for

certain cases, considering the challenges it represents in imaging dysphagic patients. Additionally, we have suppressed the T2wi TSE-DB sequence in static images due to its longer duration and the potential difficulty for patients to maintain breath-holding.

This preliminary study has some limitations. The major limitation of our study is the limited number of patients. As a consequence, we did not analyze esophageal and gastro-esophageal junction lesions separately nor did we examine the different histology individually. A histopathological reference correlation was only possible in a few cases as the majority of patients have received neoadjuvant treatment in accordance to European recommendations [3]. This study is a prospective study with a short follow-up period at this time, which may not allow statistical significance in measuring prognostic outcomes. We focused on T-stage assessment to consider the advantage of the addition of cine MR. The lack of consideration of N-staging could be a bias in the evaluation of outcomes.

A multicentric study including a larger number of patients and a longer follow-up period may be needed to confirm our results.

5. Conclusion

MRI is accurate for T-staging of EC. The addition of cine MRI increases T-staging diagnostic performance, diagnostic confidence, and inter-reader agreement for differentiating T1-T3 from T4 stages and has the potential to determine the involvement of the circumferential resection margins.

CRediT authorship contribution statement

Laura Haefliger: Writing – review & editing, Writing – original draft, Visualization, Project administration, Investigation, Formal analysis, Data curation. **Mario Jreige:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation. **Céline Du Pasquier:** Formal analysis, Data curation.

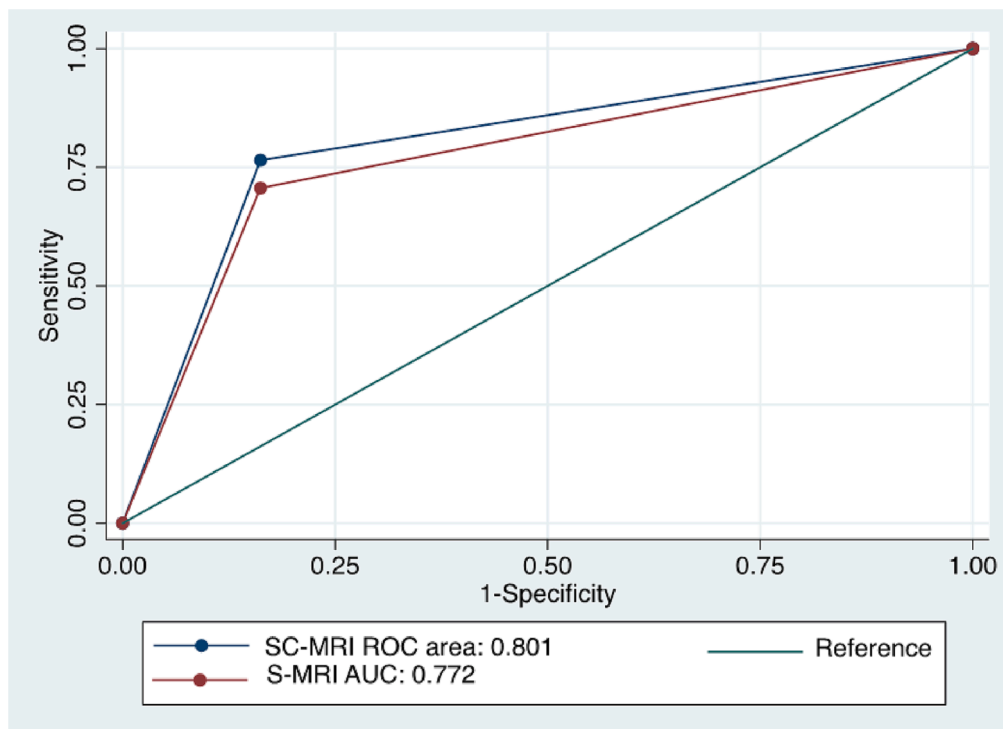


Fig. 5. ROC curves comparing performance of SC-MRI and S-MRI in distinguishing T2-T3 from T4 stages, AUC respectively of 0.801 and 0.772. *Abbreviations:* ROC: Receiver operating characteristic; S-MRI: Static MRI; SC-MRI: Static + Cine MRI; AUC: Area under the curve.

Jean-Baptiste Ledoux: Software, Data curation. **Dorothea Wagner:** Investigation and Review and editing. **Styliani Mantziari:** Visualization, Validation, Project administration, Investigation, Data curation, Review and editing. **Markus Schäfer:** Visualization, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization, Review and editing. **Naik Vietti Violi:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Data curation. **Clarisse Dromain:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejrad.2023.111001>.

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