

Endorectal Ultrasonography in Rectal Cancer

A Preliminary Barbadian Experience

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ABSTRACT

Preoperative staging of rectal cancer assists in surgical decision making regarding the suitability of curative local excision as well as in the selective use of preoperative adjuvant radiation and chemoradiation, both of which have been shown to reduce the incidence of loco-regional cancer recurrence substantially. Most colorectal units employ endorectal ultrasound (ERUS) in the assessment to define tumour depth (T) and nodal (N) status. The preliminary Barbadian experience of 40 such cases showing an accuracy for T stage of 85% and for N stage of 50% in keeping with international reports is presented. The interpretation and limitations of this technology are presented.

La Ultrasonografía Endorectal en el Cáncer del Recto

Una Experiencia Preliminar Barbadiana

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RESUMEN

La estadificación preoperatoria del cáncer rectal ayuda en la toma de decisiones en relación con la conveniencia de la excisión local curativa, así como en el uso selectivo de la radiación adyuvante preoperatoria y la quimiorradiación, las cuales han probado su eficacia en cuanto a reducir sustancialmente la incidencia de la recurrencia del cáncer loco-regional. La mayor parte de las unidades colorectales emplean el ultrasonido endorectal (UER) en la evaluación para definir la profundidad del tumor (T) y el estatus nodal (N). Se presenta la experiencia preliminar barbadense en 40 de estos casos, que muestran una precisión del 85% para el estado T y del 50% para el estado N en correspondencia con los reportes internacionales. Se presentan la interpretación y las limitaciones de esta tecnología.

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INTRODUCTION

There has been a relatively recent trend towards routine preoperative staging of rectal cancer (1) with an emphasis on the use of endorectal ultrasonography (ERUS) for those tumours within range of an endorectal probe (2). With ERUS, the aims of accurate staging include the ability to distinguish between T 1 and T 2 tumours, assisting patient selection for local resectional procedures with curative intent (3) as well as to define those patients with nodal or locally advanced disease who are likely to benefit from neo-adjuvant chemoradiation (4). Several modalities are available for use in low rectal tumours, including experienced digital rectal examination (5), computed tomography (6), endorectal ultrasono-

graphy (7), three-dimensional reconstructed endorectal sonography (8), endoluminal magnetic resonance imaging (9, 10) and high-resolution surface magnetic resonance imaging (11).

The advantages of ERUS include its ease of use, its portability and its repeatability for office-based surgical decision-making in the tailoring of rectal cancer treatment as well as its provision of important information to the surgeon regarding the suitability of first-up total mesorectal excision (12). This study is the first in the Caribbean to assess the staging accuracy of ERUS in rectal cancer in the assessment of tumour depth and lymph node status in comparison with the histological findings of the resected specimen.

SUBJECTS AND METHODS

Between May 2002 and May 2004, 50 patients were referred to a Coloproctology Unit at the Queen Elizabeth Hospital, Barbados, with histologically confirmed rectal cancer. Of these 50 patients, 40 cases underwent preoperative endorectal

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ultrasonography (ERUS) and these 40 patients are the subject of analysis. These patients consisted of 22 males and 18 females with a total mean age of 58.2 years (range 36–80 years). Four patients, because of advanced disease on presentation, underwent neo-adjuvant chemoradiation (Infusional 5-fluorouracil 425 mg/m² with leukovorin 20 mg/m² and either 45 or 60 c Gy over six weeks) with two further patients receiving short course preoperative adjuvant radiotherapy (25 c Gy over five days followed by surgery at fourteen days). Four additional patients had local excision only of their tumours and were assessed for tumour depth (T) status only.

Each examination was performed by the same person (APZ) within two weeks prior to surgery using a Bruel-Kjaer 7.5 MHz 1101 Merlin scanner (B-K, Copenhagen DK) with a 360° rotating probe head after a preliminary enema. In each case, an attempt was made to cannulate the tumour under vision using a rigid rectoscope and then to pass the probe through the rectoscope to gain access to the rostral extent of the tumour. The ultrasonographic rating of tumour depth (T) and nodal (N) status were based on the classification of Beynon *et al* (13) where *u T 1* represents a tumour confined to the mucosa and submucosa, *u T 2* is a tumour confined to the rectal wall without interruption of the outer rectal surface, *u T 3* is a growth penetrating the rectal wall with clear invasion into the hyperechoic perirectal fat and *u T 4* represents a case where there is endosonographic evidence of surrounding organ infiltration (eg the prostate, seminal vesicle or vaginal wall). An example of each stage is shown in Figs. 1–4. An attempt was made to distinguish those cases of T 2 tumours where there was a scalloped margin pushing into perirectal fat from those T 3 cases with finger-like projections infiltrating the hyperechoic fatty tissue around the rectum.

Lymph nodes were generally sought above the main tumour mass and were considered as involved if they were uniformly hypoechoic with smooth margins as described by Kumar and Scholefield (14). Predicted T and N status as defined by ERUS were compared with the histopathologic classification of resected tumours in accordance with the UICC (Union Internationale Contre le Cancer) TNM classification (15). T status sensitivity and N status sensitivity, specificity, positive predictive value, negative predictive value and accuracy are reported.

RESULTS

Figures 1–4 show examples of the ERUS appearances of the different T stages of rectal cancer. Table 1 shows T status as predicted by ERUS when related to the resection histology. Of the 40 patients examined, 60% had T 3 lesions, 25% T 2 tumours, 10% T 1 cancers and 5% T 4 tumours. The overall sensitivity for tumour depth (T) prediction by ERUS was 85% with two cases overstaged as T 4 lesions (when in fact they were T 3 cases) and four patients understaged as T 2 lesions which turned out to be T 3 cases (overall under- and



Fig. 1: An example of a villous adenoma which shows submucosal infiltration (markers) and which was confirmed after local endoanal excision as a T1 adenocarcinoma. The submucosa appears as a hyperechoic line (arrows) and malignant diagnosis is made by following this line to assess its integrity for breaks as shown.



Fig. 2: An example of a T 2 tumour showing a scalloped edge (arrowhead) which pushes into the hyperchoic perirectal fat (*) but does not invade this layer. The T 2/T 3 distinction can be particularly difficult. The outer thin hypoechoic line is the layer of the muscularis propria (arrow) which in this case is expanded by the lobulated tumour.

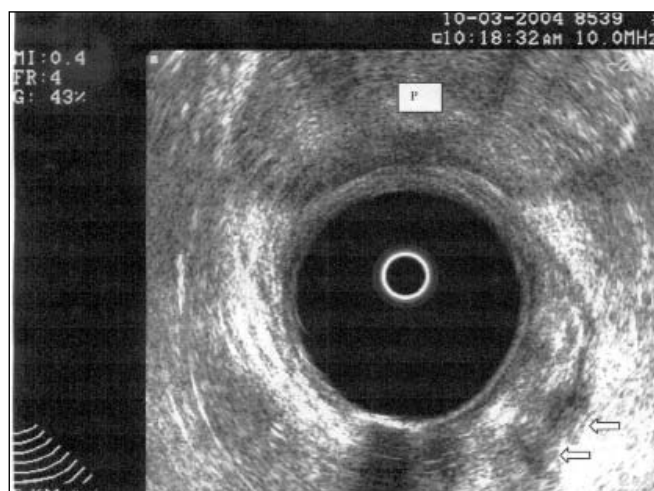


Fig. 3: An example of a T 3 invasive tumour where fingerlike projections (arrowheads) are seen infiltrating the hyperechoic perirectal fat. The prostate (P) is shown anteriorly.

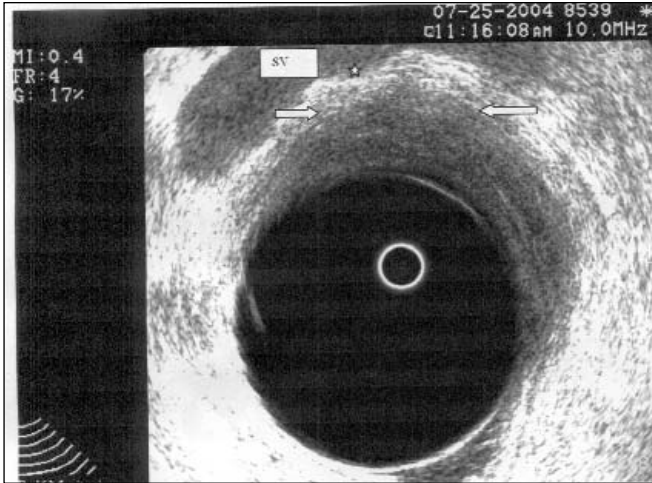


Fig. 4: An example of an anterior T 4 tumour (arrowheads) extending into the right seminal vesicle (SV). The point of invasion is shown by the star symbol.

Table 1: Comparison of the T status of rectal tumours (n = 40) using ERUS with resection histology

Ultrasonic Staging	Histopathologic Staging				
	pT				
uT	T1	T2	T3	T4	Total
T1	4	–	–	–	4
T2	–	10	4	–	14
T3	–	–	18	–	18
T4	–	–	2	2	4
Total	4	10	24	2	40

overstaging was 15%). The accuracy for T 3 staging was 81.8% (18/22). Of the four patients who underwent neo-adjuvant chemoradiation and the two patients who had short-course preoperative radiation, two in the neo-adjuvant group had an ERUS which predicted T 4 status (with seminal vesicle infiltration) but who turned out to have T 3 tumours on resection. Both had extensive xantho-granulomatous reaction in their tumour indicative of chemoradiation response represented as a loss of the normal rectal layers typically evident on ERUS.

Table 2 shows the ERUS/histology comparison for N status in cases where nodes could be assessed (36 patients), resulting in a sensitivity of 75% (18/24), a specificity of 66.7% (8/12), a positive predictive value of 81.8 % (18/22), a negative predictive value of 57.1% (8/14) and an accuracy of 50% (18/36). An ERUS case showing multiple pararectal lymphadenopathy is shown in Fig. 5. Overstaging by ERUS of N status occurred in four cases in which on reassessing these ultrasounds, in two there was difficulty in distinguishing pararectal vessels from lymph nodes. There were six

Table 2: Comparison of the N status of rectal tumours (n = 36) using ERUS with resection histology

Ultrasonic Staging	Histopathologic Staging		
	p N		
uN	pN -	pN+	Total
uN –	8	6	14
uN +	4	18	22
Total	12	24	36

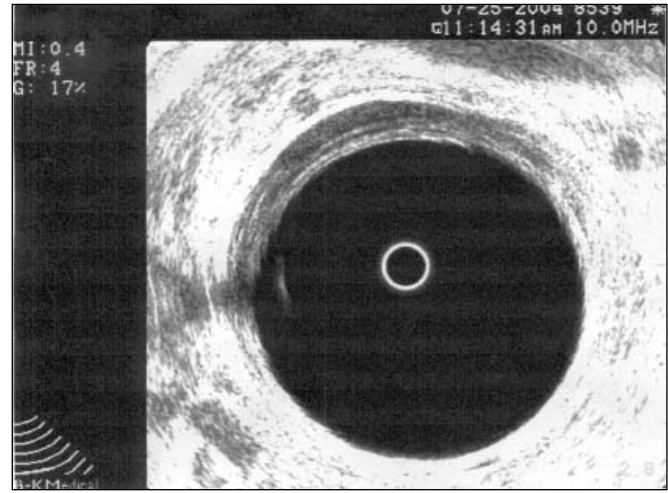


Fig. 5: Endorectal ultrasound image of malignant pararectal lymph nodes.

false negative nodal cases on ERUS where in four patients there was an inability to adequately cannulate a stenotic tumour and in a further two cases the rostral extent of the tumour exceeded the limits of the endorectal probe. The histological nodal status in all six patients receiving pre-operative adjuvant or neo-adjuvant therapies was equivalent to that predicted on ERUS staging.

DISCUSSION

This small study is the first from the Caribbean assessing the routine preoperative use of endorectal ultrasonography (ERUS) in rectal cancer, showing an acceptable accuracy for the prediction of tumour depth (T status) of 85% and an accuracy for the prediction of malignant lymphadenopathy (N status) of 50%. The overall accuracy for the prediction by ERUS of tumour depth in this study was comparable to those of other reports which have ranged between 69% and 93% (6–8).

The clinical importance for accurate preoperative staging of tumour depth in rectal cancer lies in the ability to differentiate T 1 from T 2 tumours where there would be facility for curative local therapies (29) and in the delineation of more locally advanced cases where the utilization of pre-operative adjuvant and neo-adjuvant (downstaging) therapies would normally be implemented (30, 31). The literature has

Table 3: Reported results of the assessment of tumour depth (T) and nodal status (N) of rectal cancer by ERUS

Author (Reference)	Year	Number *	T Accuracy (%)	Overstaging (%)	Understaging %	N Accuracy (%)
Hildebrandt and Feifel (18)	1985	25	92			N S
Beynon <i>et al</i> (20)	1987	100	93			N S
Rifkin <i>et al</i> (19)	1989	102	67	50		
Glaser <i>et al</i> (21)	1990	117	90			80
Katsura <i>et al</i> (24)	1992	120	92	8.3	5.3	72.3
Herzog <i>et al</i> (25)	1993	152	89	10.2	0.8	80.2
Fedayev <i>et al</i> (26)	1995	132	91	3.7	3.7	54.5
Zrihen <i>et al</i> (27)	1996	62	84			71
Genna <i>et al</i> (17)	2000	42	81			71.4
Garcia- Aguilar <i>et al</i> (7)	2002	545	69	18	13	64
Nesbakken <i>et al</i> (23)	2003	91	74			65
Hsieh <i>et al</i> (22)	2003	67	88	9	3	73
Mackay <i>et al</i> (28)	2003	356	89			66
Bali <i>et al</i> (16)	2004	33	79	10	10	59
Present Series	2005	40	85	5	10	50

* Number of patients assessable

N S = Not stated

not been supportive of the T1/T2 distinction using ERUS (32) although it is valuable in the demonstration of submucosal infiltration which may preclude local excision and in minimally invasive lesions of the submucosa which have been shown less often to have malignant lymph nodes (33), as well as in the distinction (as in one of the cases) between a villous adenoma and an early rectal carcinoma (34, 35).

The T 2/T 3 distinction on ERUS is also of great clinical importance, since a confident diagnosis of a T 3 lesion will more likely lead to preoperative adjuvant therapy, (usually in the form of short-course radiation) in those tumours where there is clear infiltration of the perirectal fat

(36, 37). This distinction can be ultrasonographically difficult and relies on the ability (as shown in Figs. 2 and 3) to differentiate between a pushing and an infiltrative margin, an effect which may occur over a very short distance. This will account in most papers for cases of both over- and understaging of the *T* status in which the vast majority of misstaged tumours are histologically in the T 3 category (16). The consequences of understaging represent more of a threat to cancer-specific survival where the ERUS is used in surgical decision making than overstaging does where unnecessary radiation may be utilized. The results of the present study, in terms of significant under- or overstaging of the tumour depth with ERUS (15%), fall within the levels reported by other groups (7, 38–40) where overstaging may be a feature of coincident peritumoural desmoplasia resulting in T 2 tumours being reported as T 3 tumours (17, 41). This effect may also be partly contributed to by the tumour locale when those tumours located in the lower rectum (< 6 cm from the anal verge) may afford a less optimal interpretation of the rectal wall layers (42). This level of accuracy will also be vital in the prediction of circumferential resection margin involvement, which could preclude a first-up total mesorectal excision and mandate preoperative adjuvant therapy (43, 44). Interpretation of the depth of residual rectal wall infiltration in the post-therapeutic rectum is also difficult, when high-dose radiation prevents adequate endosonographic separation of the rectal wall layers (45) and when pre-treatment ERUS may not correlate with post-resectional histology if there has been a significant clinical response to chemoradiation (46). As in our cases, the *T* status after such therapy is unreliable as there is no clear association between the post-treatment histological *T* stage and formal endosonographic grading systems of tumour regression (47).

The reported accuracy for prediction of *N* status ranges from 50% (present series) to 80% (25). Inherent difficulties in the prediction of involved lymph nodes arise partly as a result of the ultrasonic technology itself and partly because of tumour characteristics. Lymph nodes both involved and uninvolved with tumour may lie beyond the focal distance of the probe, and since the majority of nodes tend to lie proximal to the main tumour mass, they may not be recognized in those cases where luminal distortion prevents adequate passage of the endorectal assembly through the tumour. With respect to the pathological features of perirectal nodes, improved fat clearance histopathological techniques reveal more small lymph nodes (48) when up to 20% of nodes may have a maximal diameter < 3 mm (49) and when up to two-thirds of metastatic deposits within nodes are smaller than 5 mm in size (50). These types of lymph nodes are less likely to be visualized with ERUS, where prediction of metastatic involvement is based partly on size as well as on acoustic impedance characteristics (51). In a further two cases, the appearance of nodes early on in the study showed heterogeneity of nodal internal architecture which would not in the latter part of the study be considered pathognomonic of

metastases but which were called positive as perirectal nodes were identifiable.

In conclusion, these preliminary results mirror those reported elsewhere in the world and assist in the development of preoperative adjuvant strategies which can tailor rectal cancer treatment to the individual case. Despite the fact that ERUS is a valuable tool in surgical decision making for small as well as for more advanced rectal tumours, its use is limited in stenotic lesions, in those cases subjected to a combination of local excision and radiotherapy (52), in extensive villous lesions which carpet the rectal mucosa and in proximal cancers which exceed the length of the probe. The impact of new technologies such as three-dimensional ERUS, higher frequency miniprbes and ultrasonic contrast enhancement in rectal cancer is awaited (53).

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