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The value of diffusion weighted MRI in evaluation of pancreatic lesions

Emam Mohamed Abdelaziz Abo Seif
Radio diagnosis department, Faculty of Medicine for Girls, Al-Azhar University, Egypt

Fadila Mamdouh Elsayed
Radiology department, Faculty of Medicine for Girls, Al-Azhar University, Egypt

Abdallah Abdallah Ali Elbialy*
MSc of Radiodiagnosis, MBChB, AL-Azhar University, Egypt

***Abstract*---**Pancreatic lesions are very common and the pancreatic cancer is one of the most fatal cancers. The aim of the study was to show the value of diffusion weighted MRI in evaluation of pancreatic lesions, especially pancreatic cancer and to correlate the results of DW MRI with that of pathology or tumor markers aiming to use DWI MRI as a reasonable alternative modality especially when contrast administration is contraindicated. The study included 30 patients performed in the radiology department, El-Hussein Hospital University as well as a private center. The age of the patients ranged from 27 to 76 years (mean =51.13). MR imaging was performed on high field system (1.5 Tesla) magnet units (Philips Acheiva) and siemens. The ADC value of malignant pancreatic tumors was significantly lower than that of the normal pancreas with mean values of 1.27±0.21×10-3 mm2/sec and 1.61±0.13×10-3 mm2/sec respectively. Sensitivity of DW MRI was 95.5%, specificity 75%, NPV 85.7 % and PPV 91.3%, while Sensitivity of contrast enhanced MRI was 95.5 %,specificity 62.5 %,NPV 83.3 % and PPV (positive predictive value) 87.5%. We concluded that results of DW MRI are approaching that of contrast enhanced MRI not only in detecting pancreatic neoplasms but also in detection of tumor necrosis and liver metastasis which are essential information for the clinician that reflects disease prognosis and treatment strategies.

***Keywords*---**DW MRI, ADC value, malignant pancreatic tumors, prognosis, pancreatic cancer.

Introduction

One crucial consideration in the treatment of patients suspected of having pancreatic tumors is how to proceed diagnostically. So far, ultrasonography (US) and contrast material–enhanced computed tomography (CT) have been widely used to diagnose pancreatic tumors. Pancreatic cancer has an unfavourable overall 5-year survival of about 5% and one major reason is late diagnosis. At the time of diagnosis, less than 10% of patients are candidates for the only curative treatment, surgical resection (1). More recently the use of magnetic resonance imaging (MRI) for detection of pancreatic tumors was demonstrated. In particular, faster sequences reduced motion artifacts substantially and facilitated successful characterization of pancreatic lesions (2).Diffusion-weighted imaging is based upon the principles of Brownian motion (random thermal diffusion) of small molecules in a tissue. By applying diffusion weighting to a sequence (a combination of pulses and strong gradients) one can measure the apparent diffusion coefficient (ADC) in a given tissue and thus quantify the combined effects of capillary perfusion and water diffusion (3).

Diffusion-weighted magnetic resonance imaging has been used for diagnosis of diseases of the central nervous system for two decades being a particularly important tool in the diagnosis of ischemic stroke—and the musculoskeletal system for one decade (4). The implementation of ultrafast imaging techniques, such as parallel imaging, has made DWI of the upper abdomen a feasible option and has been found to be useful in differentiation of malignant from benign liver lesions. Recent studies indicate that DWI is promising also in pancreatic imaging (5). In view of an increasing use of MRI application in diagnosis and management of the pancreatic malignancies, the purpose of our study is to show the value of diffusion weighted mri in evaluation of pancreatic lesions, especially pancreatic cancer and to correlate the results of DW MRI with that of pathology or tumor markers aiming to use DWI MRI as a reasonable alternative modality especially when contrast administration is contraindicated.

Patients and Methods

The study included 30 patients performed in the radiology department, El-Hussein Hospital University as well as a private center. The age of the patients ranged from 27 to 76 years (mean =51.13).All patients were subjected to proper history taking, then U/S and/or CT, PET CT examinations. Some of them were suspected of lesions before conventional MRI DWI. Others had contraindications to MR imaging (eg, pacemaker or metallic prostheses), and refusal to consent to the study.

Patient Preparation

atients fasted for 4 hours before the MRI examination in order to optimize visualization of the pancreaticobiliary tree.

MRI examination

MR imaging was performed on high field system (1.5 Tesla) magnet units (Philips Acheiva) and siemens. Initial imaging consisted of axial T2-weighted fast spin-echo imaging (T2-WI) with fat suppression (repetition time (TR), 2100 ms; echo time (TE), 89.2 ms; field-of view (FOV), 34.0 cm; slice thickness, 4.0 mm; matrix, 256×224), T1-weighted dynamic contrast-enhanced imaging (T1-WI) with fat suppression (fast spoiled gradient echo recalled acquisition in the steady state; TR, 210 ms; TE, 1.7 ms; FOV, 34.0 cm; flip angle, 80°; bandwidth, 31.25 kHz; , DWI was acquired through the pancreas at 20 slice locations utilizing a finger pulse-triggered diffusion-weighted single-shot spin-echo echo-planar imaging (EPI) technique (TR, time between R-peaks (R-R) ×7 ms; TE, 63.5 ms; b=0, 500 and 1000 s/mm2, RR interval, 7; trigger window, 20%; trigger delay, minimum; inter-sequence delay, minimum; cardiac phases single FOV, 34.0 cm; slice thickness, 5 mm; spacing, 1 mm; asset factor, 2; NEX, 8; matrix, 128×128). All axial images were reconstructed to 256×256 matrix images after scanning.

Imaging evaluation

The morphological features of each lesion were recorded included size, shape, margin, signal characteristics, pattern of enhancement in the dynamic imaging as well as site of the lesions. Then provisional diagnosis was reported. Second, we reviewed the diffusion images with ADC values for final radiological characterization and detection of the pancreatic lesions.

ADC calculation

The mean ADC of each lesion detected was measured by drawing a region of interest over the lesion. The ROI was traced within the boundaries of the lesion using an electronic cursor. It was manually placed such that it was smaller in size than the actual lesion and was not include adjacent normal tissue.

Laboratory Analysis

Some of patient was subjected to biopsy. The specimens were stained with hematoxylin-eosin stain for conventional histopathologic evaluation. Histologic grading was evaluated with respect to increased cellularity, nuclear crowding, disturbance of cellular polarity, failure of differentiation from the base to the surface, polymorphism, irregularity in the size of cells, variations of shape, chromatin patterns of nuclei, displaced or abnormal mitotic figures, and giant cells. Tumors were classified into three grades: G1, the least degree of anaplasia; G2, an intermediate degree of anaplasia; and G3, severe anaplasia.

Results

Table 1
Demographic features of the studied group

Characteristics	Patients group (n= 30)
Age (yrs)	

Range	27-76
Mean ± SD	51.13 ± 15.16
Sex	
Female	9 (30%)
Male	21 (70%)

30 patients were included in this study 21 males (70%) and 9 females (30%), ranging in age between 27-76 years with mean age 51.3

Table 2
Pathology or tumor markers in the studied group

	Number	Percent
Adenocarcinoma	20	66.6
Non Hodgkin's lymphoma	1	3.3
Metastasis	1	3.3
Pancreatic endocrine tumor	1	3.3
Pancreatitis,free tumor markers	3	10
Simple cyst, free tumor markers	3	10
Suppurative inflammation	1	3.3

There were 30 pancreatic cases; 20 adenocarcinoma, 1 malignant endocrine tumor, 1 metastatic,1 non hodgkin's lymphoma, 4 inflammatory, 3 simple cysts. 23 cases were malignant (73.3%), 7 cases were benign (26.7%)among them 4 cases were inflammatory(16.7%).

Table 3
Radiological diagnosis and location of metastasis in the studied group

Characteristics	Number	Percent
Radiological diagnosis		
Benign	6	20.0
Malignant	24	80.0
location of metastasis		
Renal	1	3.3
Liver	12	40.0
Lymph node	2	6.7

Out of the 30 cases 6 cases were radiologically diagnosed as benign lesions (20%) and 24 cases were diagnosed malignant (80%). Within the malignant cases liver metastasis was present in 12 of them (40%), lymph nodes in 2 of them (6.7%) and renal masses in one case(3.3%). 4 cases (13.3%) out of the 30 cases show tumor necrosis within.

Table 4
Comparison between mean ADC values of benign and malignant lesions classified according pathological diagnosis in the studied patients

Benign (n = 8)	Malignant (n= 22)	P value
2.05 ± 0.55	1.27 ± 0.21	0.001**

Data are expressed as mean ± SD. **p< 0.01= highly significant.

Table 5
Comparison between mean ADC values of normal tissue, benign and malignant lesions classified according to pathological diagnosis

Normal ADC (n= 30)	Benign (n = 8)	P value
1.61 ± 0.13	2.05 ± 0.55	0.001**
Normal ADC (n= 30)	Malignant (n= 22)	P value
1.61 ± 0.13	1.27 ± 0.21	0.001**

Data are expressed as mean ± SD. **p< 0.01= highly significant.

Table 6
ADC of metastasis in the studied group

	N	Minimum	Maximum	Mean	Std. Deviation
Renal	1	1.070	---	1.070	---
Liver	12	0.8	1.6	1.257	0.213
Lymph node	2	1.1	1.5	1.285	0.304

Mean ADC value of the liver metastasis is 1.257 x 10-3 mm2/sec ADC values ranged between 0.8×10-3 mm2/sec and1.6×10-3 mm2/sec. , in renal metastasis 1.070 x 10-3 mm2/sec and in lymph node metastasis 1.285 x 10-3 mm2/sec ADC values ranged between 1.1×10-3 mm2/sec and1.5×10-3 mm2/sec.

Table 7
Conventional (MRI) vs pathology and Diffusion vs pathology in the studied group

Characteristics		Pathology		P value
		Benign (n = 8)	Malignant (n= 22)	
Conventional	Benign (n = 6)	5 (62.5%) TN	1 (4.5%) FN	0.001**
	Malignant (n= 24)	3 (37.5%) FP	21 (95.5%) TP	
Diffusion	Benign (n = 7)	6 (75%) TN	1 (4.5%) FN	0.001**
	Malignant (n= 23)	2 (25%) FP	21 (95.5%) TP	

Data are expressed as number (percent). **p< 0.01= highly significant. TN= true negative
FN= false negative FP= false positive TP= true positive

The agreement of the conventional MRI with the pathology is as follows: in benign lesions true negative results (62.5%), false negative (4.5%), while in malignant lesions true positive results (95.5%), false positive (37.5%). The agreement of the DWI with the pathology is as follows: in benign lesions true negative results (75%), false negative (4.5%), while in malignant lesions true positive results (95.5%), false positive (25%).

Table 8
Diagnostic indices (sensitivity, specificity, PPV, NPV and efficacy) of MRI in the studied group

	Sensitivity	Specificity	PPV	NPV	Efficacy
ADC	22/22 (100%)	6/8 (75%)	22/24 (91.7%)	6/6 (100%)	28/30 (93.3%)
Conventional	21/22 (95.5%)	5/8 (62.5%)	21/24 (87.5%)	5/6 (83.3%)	26/30 (86.7%)
Diffusion	21/22 (95.5%)	6/8 (75%)	21/23 (91.3%)	6/7 (85.7%)	27/30 (90%)

PPV= positive predictive value. NPV= negative predictive value.

Sensitivity of DW MRI was 95.5%, specificity 75%, NPV 85.7 % and PPV 91.3%, while Sensitivity of contrast enhanced MRI was 95.5 %,specificity 62.5 %,NPV 83.3 % and PPV (positive predictive value) 87.5%.

Case 1:

- **Clinical history:** Fifty three old female presenting with jaundice and loss of weight.
- **MRI findings:** pancreatic head mass measuring about 5 x 3.8 cm in its axial dimensions associated with dilated intrahepatic biliary radicles. Multiple hepatic focal lesions are also noted with the largest one measuring about 2 cm in diameter. The pancreatic focal lesion displays low T1, heterogenous bright T2WI with heterogenous enhancement more appreciated in the delayed phase. The hepatic focal lesions display low T1, high T2 signal with marginal enhancement in the post contrast study.
- **On DWIs:** The lesions appear bright, and became brighter with increasing the b value. On the ADC map, the lesions turned dark, indicating restricted diffusion.
- **ADC value:** Normal pancreas: 1.8 x 10-3 mm2/sec. Pancreatic lesion: 1.3 x 10-3 mm2/sec. Metastasis: 1.2 x 10-3 mm2/sec
- **Diagnosis: Radiological:** pancreatic head carcinoma with hepatic metastatic deposits.
- **Pathological:** Ductal adenocarcinoma.

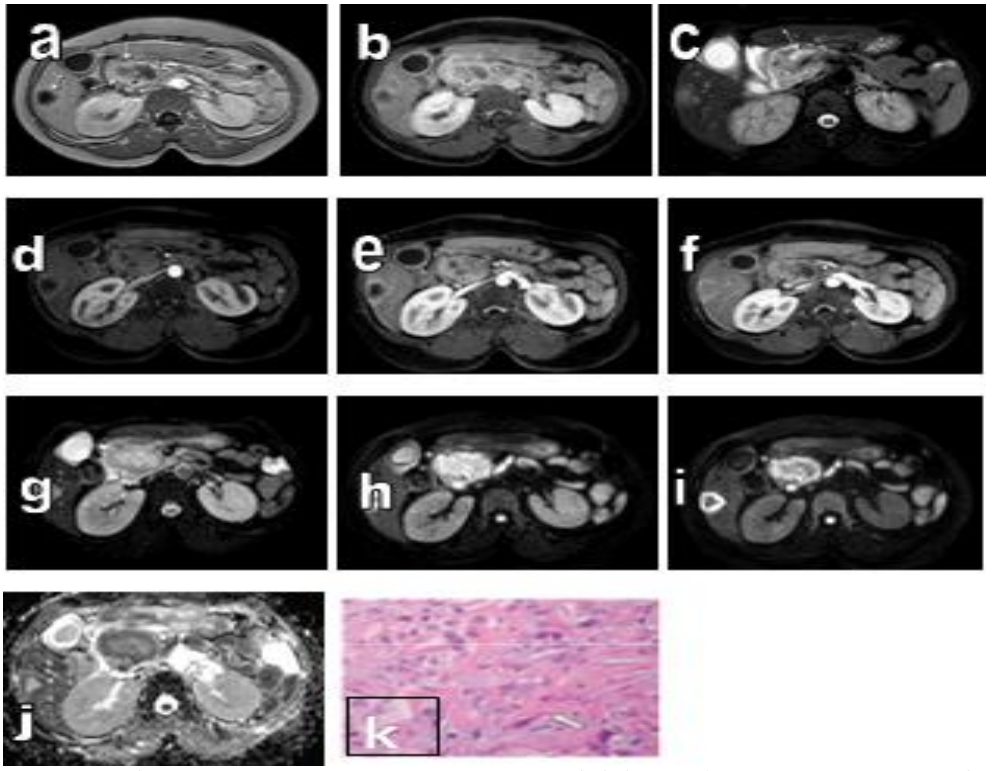

Fig 1. T1 WI, b: T1 post contrast, c: T2 SPAIR, d-f:dynamic post contrast study, g-i: DWI, b value:0, 500, 100 respectively, j: ADC. k: photomicrograph (original magnification, ×400; H-E stain) shows abundant dense fibrotic stroma composed of thick collagen bundles (arrow) infiltrated by small individual nests of adenocarcinoma cells without ducts, findings that account for the lower ADC value.

Case 2:

- **Clinical history:** 35 years old female presenting with abdominal pain.
- **MRI findings:** Pancreatic body mass measuring about 2.5 cm in diameter. It displays a low signal in T1, high signal in T2 with faint enhancement of its margin and non-enhancing central area of breaking down in the post contrast study.
- The liver shows multiple variable sized bilobar hepatic focal lesions being hypointense on T1WIs and hyperintense on T2WIs with faint marginal enhancement in the post contrast study.
- **On DWIs:** The lesions appear bright, and became brighter with increasing the b value. On the ADC map, the lesions turned dark, indicating restricted diffusion.
- **ADC value:** Normal pancreas: 1.6 x 10-3 mm2/sec, Pancreatic lesion: 1.2 x 10-3 mm2/sec. Metastasis: 1.2 x 10-3 mm2/sec
- **Diagnosis: Radiological:** pancreatic body carcinoma metastatic to the liver. **Pathological:** pancreatic ductal adenocarcinoma.

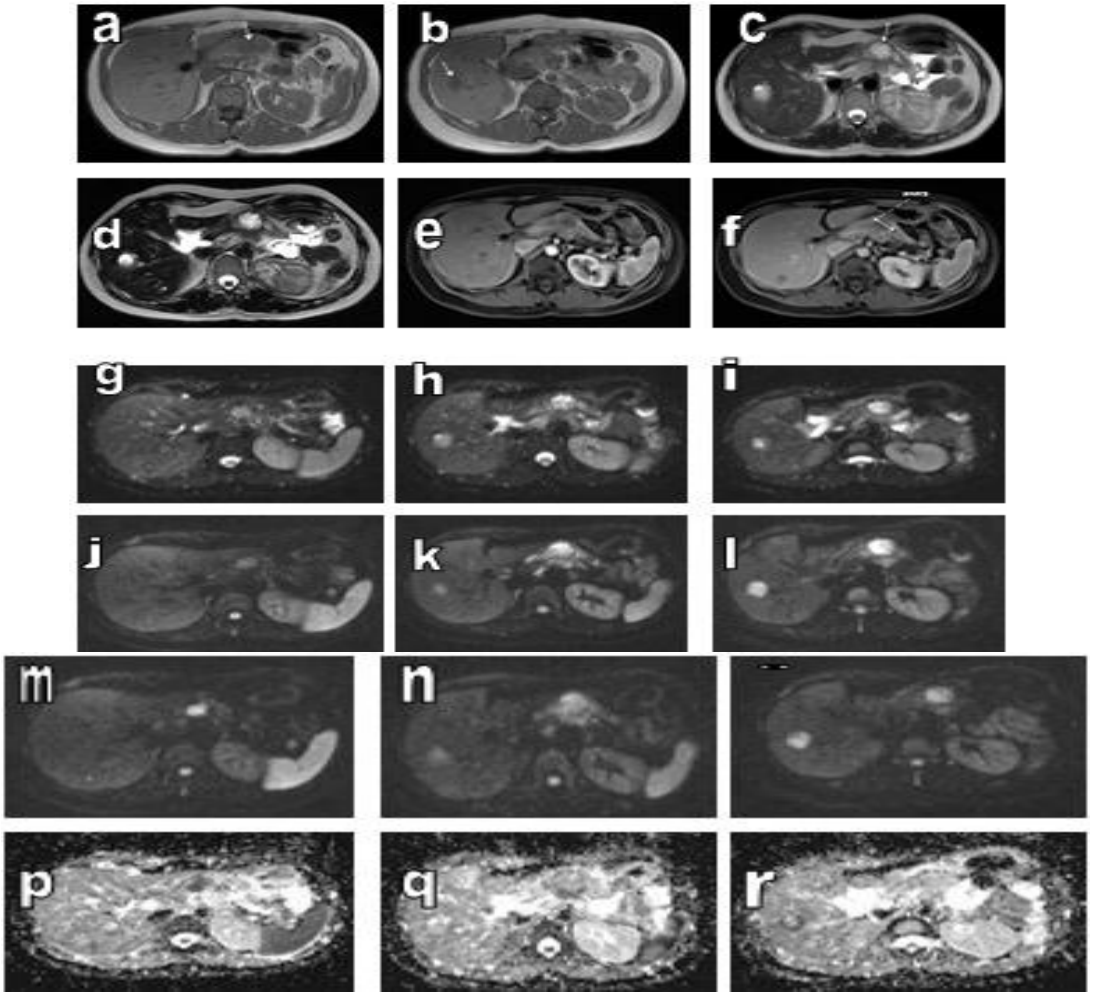

Fig 2. a-b: T1, c-d: T2, T2 SPAIR, e-f:T1 post contrast, g-p: DWI, b:0, 500, 1000, q-s: ADC

Discussion

The recent development of high-field MR systems with high gradient amplitude and the parallel imaging technique have greatly improved the diagnostic performance of DWI in the abdomen (6). In our DWI study, b values were 0, 500& 1000 sec/mm^2, with the application of parallel imaging and breath triggering technique, a satisfying image quality has been achievable on a 1.5-T scanner within an acceptable acquisition time. The major aim of the present study was to determine the usefulness of diffusion weighted imaging in diagnosis of pancreatic pathology, using ADC measurement. The current study was conducted including thirty patients, 22 malignant, 5 inflammatory and 3 benign; where in 2009 Nikolaos et al., (7) performed a study using 75 analyzed patients, 39 had no lesion found, 12 had a malignant lesion and 24 a benign lesion. The prevalence of pancreas cancer was 16%. In our study there was no significant difference in sensitivity between the two diagnostic radiology tools and a significant very good

agreement is detected between MRI and DWI. Sensitivity of DW MRI was 95.5%, specificity 75%, NPV 85.7 % and PPV 91.3%, while Sensitivity of contrast enhanced MRI was 95.5 %,specificity 62.5 %,NPV 83.3 % and PPV (positive predictive value) 87.5%.

In our study the agreement of the DWI with the pathology in our study was high, in benign lesions true negative results (75%), false negative (4.5%), while in malignant lesions true positive results (95.5%), and false positive (25%). The agreement of ADC value with the pathology in our study was also high, in benign lesions true negative results (75%), false negative (0%), while in malignant lesions true positive results (100%), and false positive (25%). While the agreement of the conventional MRI with the pathology in our study shows no significant difference than that of DWI with pathology, in benign lesions true negative results (62.5%), false negative (4.5%), while in malignant lesions true positive results (95.5%), and false positive (37.5%). These results are showing no major difference with results of Nikolaos et al., (7) in which DWI had a sensitivity and specificity of 92% and 97 % respectively with a PPV and NPV of 85% and 98% respectively compared to the results of contrast enhanced MRI in which sensitivity, specificity, PPV and NPV were 100%, 97%, 86% and 100% respectively.

Our results showed that the ADC value of malignant pancreatic tumors was significantly lower than that of the normal pancreas with mean values of $1.27\pm0.21\times10^{-3}$ mm2/sec and $1.61\pm0.13\times10^{-3}$ mm2/sec respectively findings were consistent with the results of Wen Cai et al., (6), Matsuki et al., (5) and Nikolaos et al., (7) All reported that mean ADC values of malignant pancreatic tumors were significantly lower than that of normal pancreas. Their results were as follows: Matsuki et al., (5): mean ADC values for pancreatic carcinoma was 1.43 ± 0.20 while normal pancreas mean ADC values was1.90 ± 0.05. Nikolaos et al., (7): mean ADC values for malignant pancreatic tumors was 1.40 ± 0.30 while normal pancreas mean ADC values were 1.61 (± 0.25), 1.68 (± 0.22) and 1.55 (± 0.21) x 10^{-3} mm^2/s for pancreatic head, body and tail respectively, Wen Cai et al., (6): mean ADC values for pancreatic carcinoma was (1.06 ± 0.15) while normal pancreas mean ADC values were (1.47± 0.18).

The absolute ADC values of the lesions were not similar among different studies, which is probably due to differences in techniques applied including the used b values however they reported that mean ADC values of malignant pancreatic tumors were lower than that of normal pancreas as described before. There were two false positive lesions in DWI in the present study, a suppurative inflammation with restricted diffusion and focal pancreatitis with restricted diffusion. To our knowledge, abscesses and inflammatory cells show restricted diffusion and is thought to be due to its content of high viscosity fluid with necrotic and inflammatory cells. Also in our study DWI was capable of detecting tumor necrosis. Tumor necrosis showed low signal in DWI (facilitated diffusion) and high ADC values in contrary to the viable tumor tissue which showed bright signal in DWI and low ADC values. The ability of DWI to detect tumor necrosis can be used prior to biopsy to avoid the site of necrosis and thus avoids insufficient and false negative biopsies. Liver metastasis was also detected by DWI. There are some limitations to this study. First, the small study population, so larger samples size are needed to confirm our results. Second, the study included very limited

nonmalignant cases so no reliable specificity or negative predictive value can be calculated. Last the presence of respiratory motion-related artifacts was unavoidable in uncooperative patients with an irregular respiratory rhythm. These artifacts might cause errors to ADC value measurement.

Conclusion

In this study using combined qualitative analysis of DWIs and quantitative analysis of ADC values, we concluded that results of DW MRI are approaching that of contrast enhanced MRI not only in detecting pancreatic neoplasms but also in detection of tumor necrosis and liver metastasis which are essential information for the clinician that reflects disease prognosis and treatment strategies. However, in view of limited number of cases and other limitations of the study larger studies are needed to confirm these results.

Conflict of interest: no conflicts of interest.

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