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Hybrid ^{18}F -FDG PET/CT of colonic anastomosis

A possibility to detect anastomotic leakage?

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Keywords

PET/CT, colorectal surgery, anastomotic leakage

Summary

^{18}F -fluorodeoxyglucose positron emission tomography (FDG-PET) is a known method to diagnose inflammatory processes and thus may be a promising imaging technique to detect anastomotic bowel leak. The aim of this study was to assess postoperative FDG uptake in colorectal anastomosis in patients without suspicion of active infection or anastomotic leakage. **Patients, methods:** Design of a prospective observational pilot study in order to assess normal FDG uptake in the patient anastomosis after colorectal surgery. Patients that underwent colorectal surgery with primary anastomosis received FDG-PET of the abdomen, 2–6 days postoperatively. **Results:** 35 patients met the inclusion criteria. Three patients were not scanned for various reasons. Of the remaining 32 patients, one demonstrated an

increased uptake of FDG at the site of the anastomosis. In the other 31 patients FDG uptake was negligible ($n = 17$) or scored as physiological ($n = 14$). None of the scanned patients developed a clinical relevant anastomotic leakage within the first 30 days after surgery. **Conclusion:** The present study shows that FDG uptake in colorectal anastomosis remains low within the first six days after surgery in patients without anastomotic leakage. Therefore, FDG-PET might be useful to investigate further as a tool to detect anastomotic leakage in an the early postoperative phase.

Schlüsselwörter

PET/CT, kolorektale Chirurgie, Anastomoseninsuffizienz

Zusammenfassung

Hintergrund: ^{18}F -Fluorodeoxyglukose-Positronenemissionstomographie (FDG-PET) ist ein bekanntes Verfahren zur Diagnose entzündlicher Prozesse und somit ein viel versprechen-

des bildgebendes Verfahren, um ein anastomotisches Darmleck zu erfassen. **Ziel** dieser Studie war, die postoperative FDG-Aufnahme in kolorektalen Anastomosen bei Patienten ohne Verdacht auf Infektion oder Anastomoseninsuffizienz zu beurteilen. **Patienten, Methoden:** Design einer Pilotstudie zur Beurteilung der normalen FDG-Aufnahme in Anastomosen nach kolorektaler Chirurgie. Patienten, die sich kolorektaler Chirurgie mit primärer Anastomose unterzogen, erhielten FDG-PET des Bauches, 2–6 Tage nach der Operation. **Ergebnisse:** 35 Patienten erfüllten die Einschlusskriterien, 3 Patienten wurden aus verschiedenen Gründen nicht gescannt. Von den verbleibenden 32 Patienten zeigte ein Patient eine erhöhte FDG-Aufnahme im Bereich der Anastomose. Bei den anderen 31 Patienten war die FDG-Aufnahme zu vernachlässigen ($n = 17$) oder als physiologisch anzusehen ($n = 14$). Kein Patient entwickelte eine klinisch relevante Anastomoseninsuffizienz in den ersten 30 Tagen nach der Operation. **Schlussfolgerung:** Die Ergebnisse dieser Studie zeigen, dass die FDG-Aufnahme in kolorektalen Anastomosen niedrig bleibt innerhalb der ersten sechs Tage nach der Operation bei Patienten ohne Anastomoseninsuffizienz. Daher könnte die FDG-PET nützlich sein, um weiter zu untersuchen, ob sie als Instrument zur Erfassung einer Anastomoseninsuffizienz im frühen Stadium der postoperativen Phase geeignet ist.

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Hybrid ^{18}F -FDG PET/CT kolorektaler Anastomosen – Ein Verfahren zur Entdeckung eines anastomotischen Darmlecks?

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Anastomotic leakage remains a serious adverse event after colorectal surgery. Its reported incidence varies from 1–25%. This wide range is mainly caused by the lack of a uniform definition (2, 4).

Diagnosing leaks relies on the clinical and radiographic findings. Early diagnosis and prompt treatment are essential since

delay is associated with increased mortality and morbidity (6, 8). Den Dulk et al. (5) developed a leakage-score based on clinical parameters associated with anastomotic leakage. The leakage-score was implemented in a standardized postoperative surveillance and scoring led to a reduction in delay in diagnosis and mortality.

Radiological diagnosis by means of e. g. contrast radiography or computer tomography are often advised when a leakage is suspected in a patient. However, sensitivity of both contrast radiography and computer tomography for diagnosing anastomotic dehiscence are rather low, being 65% and 54% respectively. Inter-

observer variability may be as high as 10% (7, 13).

Meller et al. (12) studied the use of ^{18}F -fluorodeoxyglucose positron emission tomography (FDG-PET) in 18 patients with postoperative fever. Sensitivity for detection of infectious and oncological foci was 100%. However, specificity was low as a result of false positive scans due to increased FDG uptake at the surgical wounds. Since leakage of bowel contents elicits at least a local inflammatory response, FDG-PET may be a promising imaging technique to improve the detection of anastomotic bowel leak, at an early stage when granulocytes and macrophages migrate to the inflammatory process. A first condition for such an application would be that the signal remains low during undisturbed healing (3, 9, 14).

Since negligible uptake of FDG at the site of the healing anastomosis is a prerequisite for early and accurate diagnosis of anastomotic dehiscence, we performed a prospective study to assess postoperative FDG uptake in colonic and colorectal anastomosis in patients without evidence of active infection or anastomotic leakage.

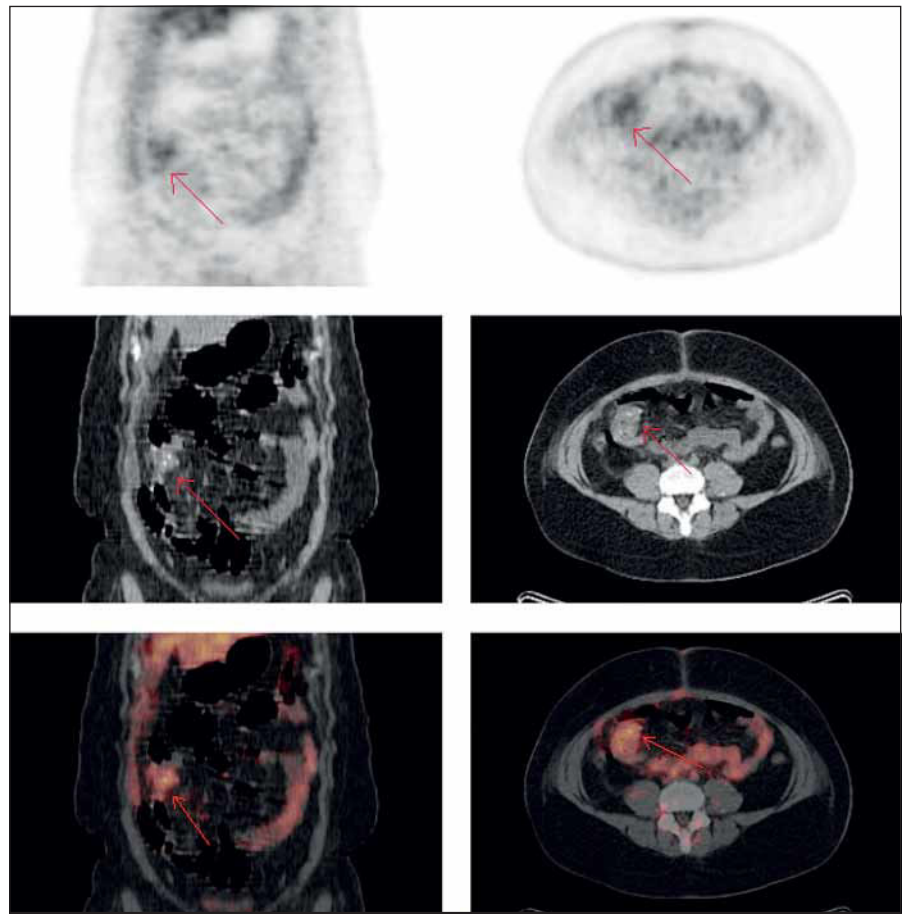


Fig. 1 FDG uptake after hemicolectomy
a) normal (→) after right hemicolectomy

Patients, material, methods

Patients

Patients who underwent a colorectal resection with primary anastomosis and gave informed consent were included in the study. The institutional review board of the Radboud University Nijmegen Medical Centre, the Netherlands, approved the study. Exclusion criteria:

- suspicion of or proven infection,
- pregnancy,
- preoperative neutropenia,
- known HIV infection,
- known hypogammaglobulinaemia (IgG <50%),
- the use of prednisolone 10 mg per day for the duration of at least two weeks in the three months prior to surgery,
- known inflammatory bowel disease,
- metastatic disease,
- uncontrolled diabetes (glucose > 10 mmol/l or the use of insulin within 6 h prior to FDG-PET).

^{18}F -FDG PET

All included patients underwent FDG-PET between two and six days after surgery. Patients fasted for at least 6 h before injection of FDG. Intake of non-caloric beverages was permitted. Intravenously administered fluids, if still necessary, contained no glucose. Hybrid PET/CT scans of the abdomen were acquired using a Biograph Duo (Siemens Medical Solutions USA, Inc.) containing a 2-slice CT scanner. A low-dose CT scan for localization and attenuation-correction purposes was acquired in the caudocranial direction from the thighs up to the diaphragm. Scanning parameters included 40 mA·s (50 mA·s for patient weight >100 kg and 60 mA·s for >120 kg), 130 kV, 5-mm slice collimation, 0.8-s rotation time, and pitch of 1.5, reconstructed to 3-mm slices for smooth co-

ronal representation. CT scans were acquired during timed unforced expiration breath-hold. No intravenous contrast was applied. For PET, a 3-dimensional (3D) emission scan of the abdomen was acquired during free breathing, 60 min after intravenous injection of 13.8 [MBq] · patient weight [kg] / (min/bed position), which is approximately 250 MBq FDG (Mallinckrodt Medical, Petten, The Netherlands) and 10–15 mg furosemide. (12) The acquisition time per bed position was 4 min for emission only. Uncorrected emission images as well as images with CT-based attenuation correction were reconstructed, both using 2 iterations, 8 subsets (for visual interpretation) or 4 iterations, 16 subsets (for quantitative interpretation), and 5-mm 3D Gaussian filter (1).

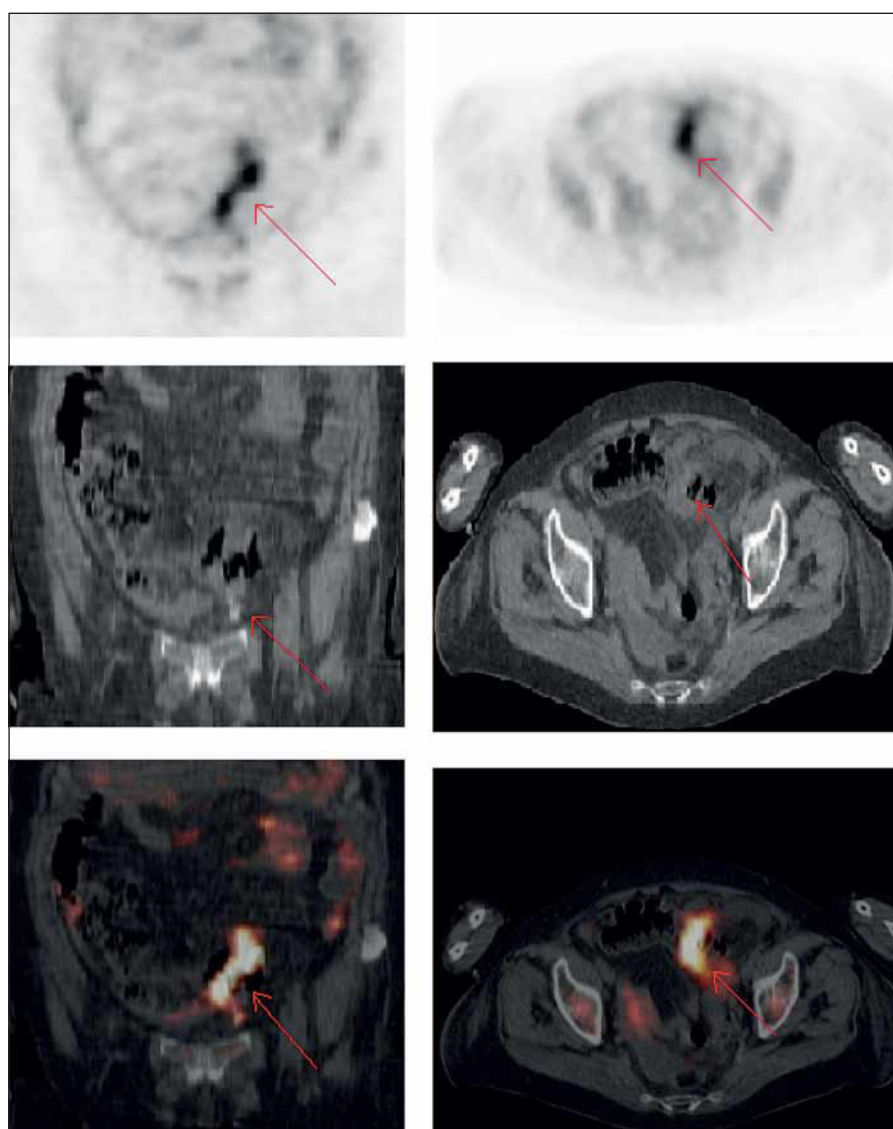


Fig. 1 FDG uptake after hemicolectomy
b) increased (→) after left hemicolectomy

Image interpretation

Two experienced nuclear medicine physicians blinded to the postoperative course and results of other diagnostic tests interpreted all FDG-scans independently. At the site of the anastomosis the degree of FDG uptake was scored as

- absent or negligible (0),
- normal physiological bowel uptake (1)
- pathologically increased (2).

Disagreements were resolved by consensus.

Results

Eighteen men and seventeen women, mean age 66.3 years (range 43–85 years), were included in the study. Three patients were classified as ASA-I (American Society of Anesthesiologists), 21 ASA-II and 11 patients were categorized ASA-III. The indication for surgery was

- (pre-)malignancy (n = 28),
- diverticulitis (n = 2) and
- restoration of bowel continuity (n = 5).

Procedures performed included

- ileocecal resection (n = 1),
- right hemicolectomy (n = 15),
- left hemicolectomy (n = 4),
- resection of the sigmoid (n = 2),
- (low) anterior resection (n = 8),
- restoration of continuity (n = 5; of which 2 ileorectal anastomosis).

Median hospital stay was 6.5 days (range 3–34). The location was the anastomosis was in the right upper abdomen in 16 patients, in the left lower quadrant in 6 and 10 were located in the pelvis region.

FDG-PET was performed after a median of 4 days (range 2–6) after the construction of the anastomosis. FDG-PET could not be performed in the early postoperative phase in 3 out of 35 included patients. In 2 patients the intravenous infusion of glucose was erroneously not discontinued. One PET could not be performed since the patient was too ill. No complication was observed during the follow-up of this patient.

17 scans were given score 0, 14 score 1.

► Figure 1a shows an example of a patient after right hemicolectomy with normal FDG uptake. In only one out of 35 scans, there was a disagreement between score 0 and 1. After consensus, it was decided that score 1 was most appropriate. So, inter-observer variability was below 3%.

One of the scans showed abnormal FDG uptake at the site of the anastomosis (score 2; ► Fig. 1b). The involved patient was an woman (age: 80 years) who was treated for a symptomatic colonic stenosis, highly suspicious for malignancy. She underwent a left hemicolectomy and resection of the proximal jejunum. The postoperative course was prolonged due to ileus, for which she required parenteral nutrition. She went home 16 days after surgery with a normal gastrointestinal function. Pathologic examination revealed Crohn's disease, without disease activity in the resection margins.

The median time between surgery and FDG-PET acquisition was four days in PET-score 0 and in PET-score 1 group. Overall morbidity in both groups did not differ neither (PET-score 0: 9/17 vs. PET-score 1: 8/14; not significant, ► Tab. 1). Three patients underwent extensive adhesiolysis: two patients had PET-score 0 and one patient had PET-score 1.

Tab. 1 Complications after surgery (absolute numbers)

complication	PET score*			total
	0	1	2	
n	17	14	1	32
ileus	2		1	3
gastroparesis		2		2
superficial surgical site infection	2			2
febris e.c.i.	2			2
phlebitis		1		1
atrial fibrillation	1	2		3
pneumonia	2			2
urinary tract infection		1		1
delirium		2		2

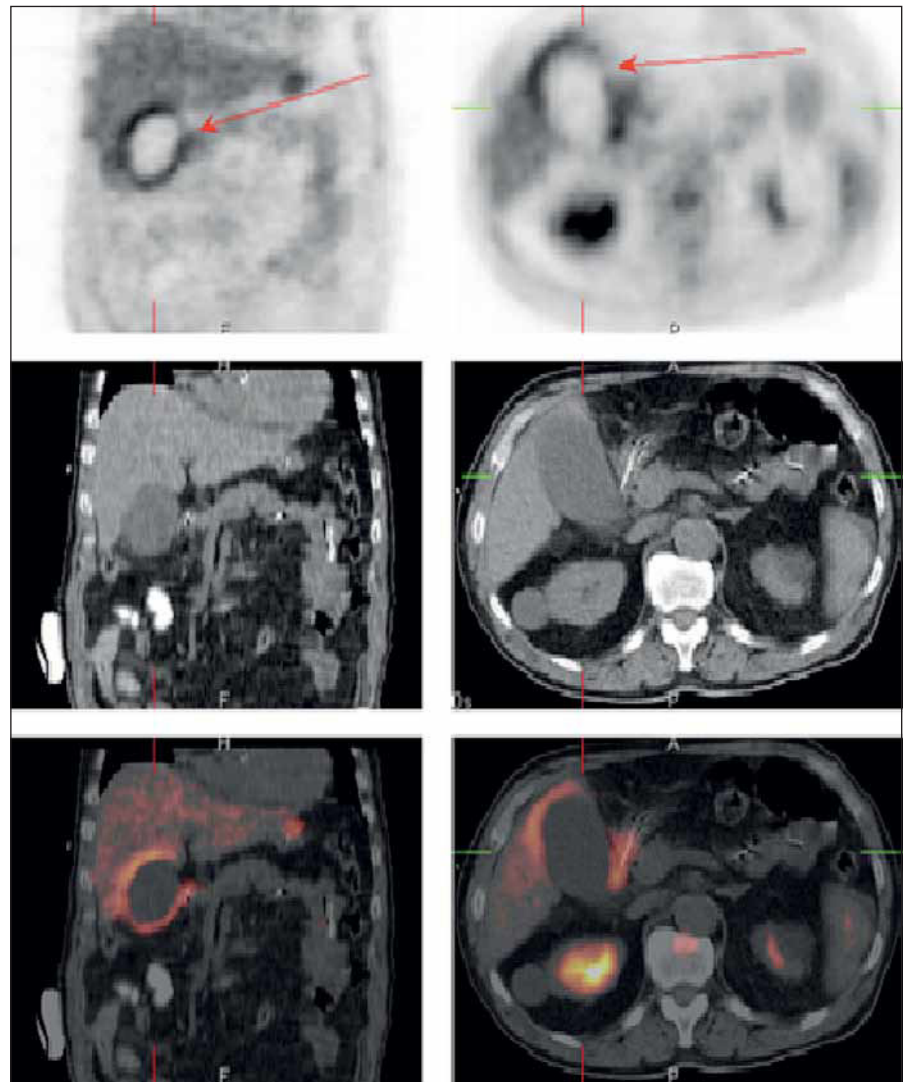
* FGD-uptake at the location of the anastomosis
absent/ negligible → PET score 0
physiological → PET score 1
pathological increased → PET score 2

Discussion

To the best of our knowledge, there are no reports on FDG-PET scanning of bowel anastomoses after colorectal surgery. The results of our study show:

FDG uptake in colorectal anastomosis is absent or physiological in the first six days after surgery.

Early diagnosis of anastomotic leakage is considered important for timely initiation of treatment. It was hypothesized that FDG-PET scanning might be helpful to diagnose anastomotic dehiscence at an early stage since uptake of FDG will probably be increased due to inflammation by leakage of bowel contents. However, healing of the bowel anastomosis itself also initiates an inflammatory response, which may interfere with the diagnostic accuracy of FDG-PET to detect anastomotic leakage at an early stage. The results of our study indicate that the normal healing process at the anastomotic site does not increase the uptake of FDG, resulting in a high specificity of FDG-PET. In only one patient pathologically increased FDG uptake at the site

**Fig. 2** Incidental finding of cholecystitis

of the anastomosis was observed. Pathology revealed Crohn's disease, but without disease activity at the resection margins. Although FDG-PET correlates well with disease activity in patients with inflammatory bowel disease, it is questionable if this is an explanation for the increased uptake in our patient since the resection margins were free of disease activity. Thus, this result has to be considered as false positive (10, 11).

The advantage of FDG-PET is that it can recognize other foci of infection that can clarify patients' complaints. We found other FDG-avid lesions in two patients who had a normal FDG accumulation at the site of the anastomosis. One patient had a cholecystitis (► Fig. 2); the other patient underwent an

adhesiolysis for dense adhesions of the colon to the abdominal wall after Hartmann's procedure for perforated diverticulitis.

Conclusion

Since uptake of FDG in a colorectal anastomosis is normal and specificity is high, FDG-PET might be a valuable diagnostic tool to detect anastomotic dehiscence in future.

Further research is needed to determine its diagnostic value, sensitivity and positive predictive value. Furthermore, it is important to define precise criteria in which cases FDG-PET is indicated. Routine scanning

after colorectal resections is not useful. If the sensitivity of FDG-PET scan proves to be high it could be a valuable diagnostic tool in high-risk cases and patients suspected for anastomotic leakage.

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Conflict of interest

The authors declare, that there is no conflict of interest.

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