Evidence-Based PET for Abdominal and Pelvic Tumours

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7.1 Introduction

Evidence-based data about the usefulness of positron emission tomography (PET) and hybrid imaging methods (PET/CT and PET/MRI) in abdominal and pelvic tumours have been collected and discussed in this chapter. These data were divided in three sections: (1) gastrointestinal tumours, (2) uro-genital tumours, (3) gynaecological tumours. Several pooled data (diagnostic and prognostic data), clinical settings (e.g. staging, restaging, treatment evaluation) and radiotracers as fluorine-18 fluorodeoxyglucose (^{18}F-FDG), radiolabelled choline and prostate-specific membrane antigen (PSMA) were considered.

7.2 PET in Gastrointestinal Tumours

Fifty-two meta-analyses on the role of PET imaging in gastrointestinal tumours have been selected [1–52]. Pooled data about PET/CT in colorectal cancer, gastric cancer, anal cancer, stromal tumours, hepato-biliary tumours, liver metastases and pancreatic cancer have been reported in Table 7.1.

7.2.1 Colorectal Cancer

Fourteen meta-analyses about ^{18}F-FDG PET/CT in colorectal cancer have been found [1–14]. Two meta-analyses evaluated the role of this imaging method in a staging setting, showing good specificity but low sensitivity [4, 13]. Similarly, two studies showed high accuracy in a restaging setting [7, 12]. Some meta-analyses assessed sub-optimal accuracy in treatment evaluation [3, 6, 8, 10, 14]. Recent meta-analyses found that focal colorectal incidental uptake at ^{18}F-FDG PET/CT is observed in a not negligible number of patients who undergo this imaging method with a high risk of malignant or premalignant lesions [2, 9]. Finally, poor predictive or prognostic role of ^{18}F-FDG PET/CT in colorectal cancer emerged [1, 5, 11].

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Table 7.1 Main findings of meta-analyses about the role of PET imaging in gastrointestinal tumours

Tumours	Authors	Topic	Pooled sensitivity	Pooled specificity	PFS HR	OS HR
Colorectal cancer	Kim et al. [1]	Prediction	0.66	0.67	–	–
	Son et al. [2]	Characterization	0.87	0.83	–	–
	Rymer et al. [3]	Treatment evaluation	–	–	–	–
	Ye et al. [4]	T staging	0.73	0.99	–	–
	Xia et al. [5]	Prognosis	–	–	0.45	0.36
	Maffione et al. [6]	Treatment evaluation	0.73	0.77	–	–
	Yu et al. [7]	Restaging	0.94	0.94	–	–
	Li et al. [8]	Treatment evaluation	0.81	–	–	–
	Treglia et al. [9]	Characterization	–	–	–	–
	Li et al. [10]	Treatment evaluation	0.78	0.81	–	–
	Krug et al. [11]	Prognosis	–	–	0.70	0.39
	Lu et al. [12]	Restaging	0.90	0.80	–	–
	Lu et al. [13]	N staging	0.43	0.88	–	–
	Zhang et al. [14]	Treatment evaluation	0.78	0.66	–	–
Gastric cancer	Luo et al. [15]	N staging	0.52	0.88	–	–
	Wu et al. [16]	Prognosis	–	–	1.70	1.72
	Li et al. [17]	Restaging	0.85	0.78	–	–
	Zou et al. [18]	Restaging	0.86	0.88	–	–
	Cui et al. [19]	Staging	0.92	0.89	–	–
	Wu et al. [20]	Restaging	0.78	0.82	–	–
	Seevaratnam et al. [21]	N staging	0.40	0.98	–	–
Anal cancer	Sadeghi et al. [22]	Prognosis	–	–	5.36	5.87
	Albertsson et al. [23]	RT planning	–	–	–	–
	Mahmud et al. [24]	N staging	0.93	0.76	–	–
	Jones et al. [25]	Staging	0.99	–	–	–
	Caldarella et al. [26]	N staging	0.56	0.90	–	–
Stromal tumours (GIST)	Kim et al. [27]	Predictive value	0.88	0.88	–	–
	Hassanzadeh et al. [28]	Treatment evaluation	0.90	0.62	–	–
Hepato-biliary tumours	Liao et al. [29]	Restaging	0.64	0.95	–	–
	Hu et al. [30]	Staging	0.80	0.70	–	–
	Sun et al. [31]	Prognosis	–	–	7.2	2.1
	Annunziata et al. [32]	Staging	0.87	0.78	–	–
	Zhang et al. [33]	Staging	0.91	0.81	–	–
	Bertagna et al. [34]	Staging	–	–	–	–
	Chou et al. [35]	M staging	0.82	–	–	–
	Annunziata et al. [36]	Staging	0.81	0.82	–	–
	Lin et al. [37]	M staging	0.77	0.98	–	–

Table 7.1 (continued)

Tumours	Authors	Topic	Pooled sensitivity	Pooled specificity	PFS HR	OS HR
Liver metastases	Choi et al. [38]	Staging	0.74	0.94	–	–
	Samim et al. [39]	Treatment evaluation	0.84	0.92	–	–
	Maffione et al. [40]	Staging	0.93	0.93	–	–
	Deng et al. [41]	Staging	0.84	0.99	–	–
	Zheng et al. [42]	Treatment evaluation	0.79	0.84	–	–
	Poulu et al. [43]	Restaging	0.73	0.85	–	–
	van Kessel et al. [44]	Treatment evaluation	0.54	n/a	–	–
Pancreatic cancer	Daamen et al. [45]	Restaging	0.88	0.89	–	–
	Wang et al. [46]	M staging	–	–	–	–
	Zhu et al. [47]	Prognosis	–	–	1.90	1.70
	Toft et al. [48]	Staging	0.89	0.70	–	–
	Best et al. [49]	Characterization	0.92	0.65	–	–
	Rijkers et al. [50]	Characterization	0.90	0.76	–	–
	Wang et al. [51]	Staging/prognosis	0.91	0.81	–	2.39
	Wu et al. [52]	Staging	0.87	0.83	–	–

HR hazard ratio, *PFS* progression free survival, *OS* overall survival

7.2.2 Gastric Cancer

Seven meta-analyses analysed the role of ^{18}F-FDG PET/CT in gastric cancer [15–21]. Three meta-analyses found a good accuracy in a staging setting, but with low sensitivity in detecting lymph nodal (N) involvement [15, 19, 21]. Conversely, other meta-analyses showed a good accuracy in a restaging setting [17, 18, 20]. Only one evidence-based article demonstrated a suboptimal prognostic value of ^{18}F-FDG PET/CT in gastric cancer [16].

7.2.3 Anal Cancer

Five meta-analyses about ^{18}F-FDG PET/CT in anal cancer have been included [22–26]. Some meta-analyses evaluated the role in a staging setting, with discordant accuracy values [24–26]. One meta-analysis found a strong prognostic power of ^{18}F-FDG PET parameters for progression free survival (PFS) and overall survival (OS) [22]. Finally, another meta-analysis assessed the role of ^{18}F-FDG PET/CT in radiotherapy planning [23].

7.2.4 Stromal Tumours (GIST)

Two meta-analyses about the role of ^{18}F-FDG PET/CT in treatment evaluation and prediction of malignant potential in patients with GIST have been found and included [27, 28], suggesting a role of this imaging method in these settings.

7.2.5 Hepato-biliary Tumours

Nine meta-analyses about ^{18}F-FDG PET/CT in hepatic and biliary tumours have been included [29–37]. Some meta-analyses found a role of ^{18}F-FDG PET/CT in a staging setting, in particular about detection of distant metastases (M) [30, 32, 33, 35–37]. One meta-analysis found low sensitivity in a restaging setting [29]. Conversely, another meta-analysis showed high prognostic power for PFS by ^{18}F-FDG PET/CT in hepato-biliary tumours [31]. Beyond ^{18}F-FDG, radiolabelled choline PET/CT showed a good detection rate of tumour lesions in patients with hepatocellular carcinoma [34].

7.2.6 Liver Metastases

Seven meta-analyses about the role of ^{18}F-FDG PET/CT in detecting liver metastases from different primary tumours have been found [38–44]. Some studies showed high specificity in a staging setting [38, 40, 41]. One study found a sub-optimal sensitivity also in a restaging setting [43]. The role in treatment evaluation improved in a recent meta-analysis [42, 44].

7.2.7 Pancreatic Cancer

Eight meta-analyses about ^{18}F-FDG PET/CT in pancreatic cancer have been published and included [45–52]. Interestingly, some papers showed good sensitivity in a staging setting [46, 48, 51, 52]. Two studies demonstrated a good accuracy of this imaging method in characterizing pancreatic lesions [49, 50]. Finally, two meta-analyses found a prognostic power for ^{18}F-FDG PET/CT in pancreatic cancer [47, 51].

7.3 PET in Gynaecological Tumours

Thirty-three meta-analyses on the role of ^{18}F-FDG PET imaging in gynaecological tumours have been selected [53–82]. Pooled data about ^{18}F-FDG PET/CT in cervical cancer, endometrial cancer, ovarian cancer and peritoneal carcinomatosis have been reported in Table 7.2.

7.3.1 Cervical Cancer

Twelve meta-analyses about the role of ^{18}F-FDG PET/CT in cervical cancer have been included [53–64]. Some studies evaluated the role of ^{18}F-FDG PET/CT in staging cervical cancer, showing low sensitivity and high specificity in N staging [53, 56, 64]. Several studies evaluated the role of ^{18}F-FDG PET/CT in a restaging setting, with high values of sensitivity and specificity [55, 58–61, 63]. Some meta-analyses found a prognostic role of ^{18}F-FDG PET/CT in cervical cancer [54, 57, 62].

7.3.2 Endometrial Cancer

Seven meta-analyses about the role of ^{18}F-FDG PET/CT in endometrial cancer have been included [65–71]. Some meta-analyses evaluated the role of ^{18}F-FDG PET/CT in a staging or restaging setting, showing good values of sensitivity and specificity [65, 68–71]. Conversely, one meta-analysis showed low sensitivity in N staging [71]. Finally, some meta-analyses showed a prognostic role of ^{18}F-FDG PET/CT for PFS [66, 67].

7.3.3 Ovarian Cancer

Six meta-analyses about ^{18}F-FDG PET/CT in ovarian cancer have been found [72–77]. Some meta-analyses showed high accuracy of this imaging method in a restaging setting [74–76]. Conversely, some meta-analyses showed sub-optimal sensitivity in N and M staging [72, 77]. Only one meta-analysis showed a good prognostic power of ^{18}F-FDG PET/CT in ovarian cancer, with particular regard to OS [73].

7.3.4 Peritoneal Carcinomatosis

Three meta-analyses were focused on the role of ^{18}F-FDG PET/CT in peritoneal carcinomatosis, showing good values of sensitivity and specificity of this method in this setting [78–80].

7.3.5 PET/MRI

Finally, recent studies evaluated the role of ^{18}F-FDG PET/MRI in gynaecological malignancies, showing optimal diagnostic accuracy values [81, 82].

Table 7.2 Main findings of meta-analyses about the role of PET imaging in gynaecological tumours

Tumours	Authors	Topic	Pooled sensitivity	Pooled specificity	PFS HR	OS HR
Cervical cancer	Ruan [53]	N staging	0.72	0.96	–	–
	Han [54]	Prognosis	–	–	5.89	6.62
	Zhou [55]	Restaging	0.97	0.81	–	–
	Liu [56]	N staging	0.66	0.96	–	–
	Sarker [57]	Prognosis	–	–	2.66	2.45
	Xiao [58]	Restaging	0.94	0.92	–	–
	Ding [59]	Restaging	0.92	0.94	–	–
	Meads [60]	Restaging	0.95	0.87	–	–
	Chu [61]	Restaging	0.87	0.97	–	–
	Zhao [62]	Prognosis	–	–	–	2.06
	Meads [63]	Restaging	0.92	0.88	–	–
	Gong [64]	N staging	0.68	0.97	–	–
Endometrial cancer	Bollineni [65]	Restaging	0.95	0.91	–	–
	Pan [66]	Prognosis	–	–	3.33	1.31
	Ghooshkhanei [67]	Prognosis	–	–	7.4	–
	Kakhki [68]	Staging	0.82	0.90	–	–
	Sadeghi [69]	Restaging	0.92	0.96	–	–
	Kadkhodayan [70]	Restaging	0.96	0.92	–	–
	Chang [71]	N staging	0.63	0.95	–	–
Ovarian cancer	Han [72]	M staging	0.72	0.93	–	–
	Han [73]	Prognosis	–	–	2.50	8.06
	Suppiah [74]	Restaging	0.90	0.90	–	–
	Xu [75]	Restaging	0.92	0.91	–	–
	Limei [76]	Restaging	0.87	0.90	–	–
	Yuan [77]	N staging	0.73	0.97	–	–
Peritoneal carcinomatosis	Kim [78]	Diagnosis	0.87	0.92	–	–
	Li [79]	Diagnosis	0.84	0.98	–	–
	Chang [80]	Diagnosis	0.72	0.97	–	–
PET/MRI	Zheng [81]	Restaging	0.96	0.95	–	–
	Nie [82]	Staging	0.95	0.95	–	–

HR hazard ratio, *PFS* progression free survival, *OS* overall survival

7.4   PET in Uro-genital Tumours

Thirty-five meta-analyses on the role of PET imaging in uro-genital tumours have been selected [83–117]. In particular, pooled data about radiolabelled choline, PSMA and fluciclovine PET/CT in prostate cancer and ^{18}F-FDG PET/CT in bladder cancer, renal cell carcinoma, testicular and penile cancer have been included (Table 7.3).

7.4.1   Prostate Cancer

7.4.1.1   Radiolabelled Choline PET for Prostate Cancer

Several meta-analyses described a very high specificity for detection of local lymph node involvement and for detection of distant metastases of prostate cancer by using radiolabelled choline PET. Radiolabelled choline PET is also widely used in patients with suspected biochemi-

Table 7.3 Main findings of meta-analyses about the role of PET imaging in uro-genital tumours

Tumours	Authors	Tracers	Topic	Sensitivity	Specificity
Prostate cancer	Evangelista et al. [83]	Choline	N staging	0.49	0.95
	Evangelista et al. [85]	Choline	Restaging	0.85	–
	Evangelista et al. [84]	Choline	Staging	0.86	0.93
	Fanti et al. [86]	Choline	Restaging	0.89	0.89
	Guo et al. [90]	Choline	M staging	0.89	0.98
	Liu et al. [92]	Several tracers	Staging	0.83 (choline)	0.93 (choline)
	Beheshti et al. [93]	Acetate	Staging	0.75	0.76
	Ouyang et al. [94]	Several tracers	Staging	0.78 (choline)	0.90 (choline)
	Ren et al. [115]	Fluciclovine	Restaging	0.87	0.66
	Sathianathen et al. [116]	Several tracers	Restaging	0.81 (choline) 0.80 (fluciclovine) 0.76 (PSMA)	0.84 (choline) 0.62 (fluciclovine) 0.99 (PSMA)
	Shen et al. [91]	Choline	M staging	0.91	0.99
	Treglia et al. [88]	Choline	Restaging	–	–
	Umbehr et al. [87]	Choline	Staging	0.84	0.79
	Von Eyben et al. [95]	Choline	M restaging	–	–
	Wei et al. [89]	Choline	Staging	0.82	0.92
	Bertagna et al. [117]	FDG	Prediction	–	–
	Corfield et al. [96]	PSMA	Staging	–	–
	Han et al. [98]	PSMA	Management	n/a	n/a
	Kim et al. [99]	PSMA	Staging	0.71	0.95
	Pereira et al. [102]	PSMA	Restaging	–	–
	Perera et al. [100]	PSMA	Staging	0.86	0.86
	von Eyben [101]	PSMA	Staging	0.70	0.84
	Hope et al. [97]	PSMA	Restaging	0.74	0.96
Bladder cancer	Lu et al. [105]	FDG	Staging	0.90	1
	Soubra et al. [106]	FDG	Prediction	0.56	0.95
	Wang et al. [107]	FDG	Staging	0.80	0.84
	Zhang et al. [108]	FDG	Staging	0.82	0.92
	Ha et al. [104]	FDG	N staging	0.57	0.92
	Crozier et al. [103]	FDG	Staging	0.56	0.92
	Kim et al. [109]	Choline and acetate	N staging	0.66	0.89
Testicular cancer	Zhao et al. [112]	FDG	Staging	0.75	0.87
	Treglia et al. [113]	FDG	Treatment evaluation	0.78	0.86
Renal cell carcinoma	Wang et al. [111]	FDG	Staging	0.91	0.88
	Ma et al. [110]	FDG	Restaging	0.86	0.88
Penile cancer	Sadeghi et al. [114]	FDG	N staging	0.81	0.92

FDG fluorodeoxyglucose, *PSMA* prostate-specific membrane antigen

cal relapse after initial treatments, even as a guide for salvage lymph node dissection [83–87]. Additionally, PSA kinetics was shown to be strongly related to the detection rate in patients undergoing radiolabelled choline PET [88]. Similarly, high PSA trigger was shown to be an important risk factor for positive findings of radiolabelled choline PET/CT [89]. PET with radiolabelled choline is a well-established imaging tool in clinical practice for detection of bone metastases [90, 91]. Diagnostic accuracy of radiolabelled choline PET was proven to be superior than other radiotracers as ^{18}F-FDG and ^{11}C-acetate [92], even if ^{11}C-acetate PET could be

considered in patients with relapse [93]. ^{18}F-fluorocholine (FCH) PET showed higher specificity than ^{11}C-choline PET [94]. Conversely, the choice of ^{18}F-FCH or ^{11}C-choline might not affect the detection of metastases in restaging patients after primary surgery and/or radiotherapy [95].

7.4.1.2 Radiolabelled PSMA PET in Prostate Cancer

Radiolabelled PSMA PET showed higher detection rate than other imaging modalities in prostate cancer [96, 97]. It was also proven to alter significantly the clinical management of these patients [98]. Diagnostic performance of PSMA PET was high for detection of node involvement in intermediate- and high-risk prostate cancer patients [99–101]. PSA kinetics may be predictor of radiolabelled PSMA PET positivity in patients with biochemical relapse [102]. PSMA detection rate ranged from 64% to 97% when PSA trigger was over 2 ng/ml at the time of scan [97].

7.4.1.3 Fluciclovine PET in Prostate Cancer

A meta-analysis demonstrated that fluciclovine (^{18}F-FACBC) PET/CT had an 87% pooled sensitivity and 66% pooled specificity in detecting prostate cancer recurrence, being a useful imaging method in this setting [115].

7.4.1.4 Incidental ^{18}F-FDG Uptake in the Prostate

A meta-analysis demonstrated that incidental ^{18}F-FDG uptake in the prostate is observed in about 2% of ^{18}F-FDG PET/CT scans performed in male patients carrying a significant risk of malignancy. Therefore, whenever this finding is detected further investigation is warranted to exclude malignancy [117].

7.4.2 Bladder Cancer

Several evidence-based articles were focused on the clinical usefulness of ^{18}F-FDG PET/CT in patients with bladder cancer [103–109]. An over-all sensitivity and specificity of 82% and 92% was reported, respectively [108]. Sensitivity and specificity were 90% and 100%, respectively, for primary staging, and 82% and 89%, respectively, for restaging [105]. For detection of node metastases, specificity was found high, whereas sensitivity was poor [103, 104, 106]. Additionally, detection of node involvement was assessed by other radiopharmaceuticals such as ^{11}C-choline or ^{11}C-acetate [109], showing low sensitivity and moderate specificity.

7.4.3 Renal Cell Carcinoma

Values of sensitivity and specificity of ^{18}F-FDG PET/CT were 86% and 88%, respectively, for detection of recurrence [110]. If diagnostic performance of ^{18}F-FDG PET/CT for detection of recurrent renal and extra-renal lesions was assessed separately, sensitivity and specificity of extra-renal lesions was found superior than accuracy for renal lesions [111].

7.4.4 Testicular and Penile Cancer

^{18}F-FDG-PET sensitivity was non-optimal in the evaluation of patients with testicular cancer [112]. Similar results were drawn if PET was performed after chemotherapy treatment in patients with seminoma [113]. Clinical usefulness of ^{18}F-FDG PET for detection of metastatic inguinal lymph nodes in patients with penile cancer is controversial [114].

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