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Station-level 18F-FDG PET/CT for lymph node staging in gynecologic cancer: where it is reliable, where it misleads, and a two-centre analysis of discordance with histopathology

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Abstract

Objective. To evaluate the per-station diagnostic performance of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) for preoperative lymph node staging in gynecologic cancer and to characterise the pattern of discordance with histopathology.

Methods. In this retrospective two-centre diagnostic-accuracy study (reported per STARD 2015), 120 women with endometrial, ovarian, cervical or vulvar cancer underwent preoperative FDG-PET/CT followed by lymphadenectomy, with histopathology as the gold standard. Sensitivity, specificity and predictive values were derived for each nodal station. We further tested whether scan-day blood glucose was associated with false-negative findings and the neutrophil-to-lymphocyte ratio (NLR) with false-positive findings, and assessed primary-tumour SUVmax as a predictor of nodal metastasis.

Results. Across 280 stations, FDG-PET/CT was highly specific (94%) but only moderately sensitive (62.5%), performing best at the pelvic (sensitivity 71%) and worst at the para-aortic station (45%); at the common iliac station the positive predictive value was only 27%. Discordance was asymmetric, with a false-negative rate of 37.5% versus a false-positive rate of 6%. Per patient, sensitivity was 76.7% and specificity 81.1%, with high inter-reader agreement (Cohen's $\kappa = 0.81$). A higher primary-tumour SUVmax independently predicted nodal metastasis (AUC 0.73, 95% CI 0.62–0.83; $p < 0.001$). False-negative findings tended to occur at higher scan-day glucose (odds ratio 1.30 per 10 mg/dL, 95% CI 0.91–1.86; non-significant), whereas inflammatory indices were unrelated to false-positive findings.

Conclusions. A positive FDG-PET/CT nodal finding is usually reliable, whereas a negative finding does not exclude metastasis and should not replace surgical nodal staging when this would alter management. The common iliac station is particularly prone to false-positive findings; a non-significant trend linked higher scan-day glucose to false-negative findings; and a high primary-tumour SUVmax may heighten suspicion of nodal disease despite a negative nodal read.

Introduction

Gynecologic cancers represent a substantial global health burden (13), and the presence of lymph node metastasis is a key determinant of stage and of the indication for adjuvant treatment (14, 15). However, its accurate preoperative detection by imaging remains challenging. FDG-PET/CT is widely used for this purpose and exhibits a characteristic diagnostic asymmetry: its specificity is high, so that positive findings are generally reliable, whereas its sensitivity is limited and metastatic disease is frequently missed. In the largest meta-analysis in endometrial cancer (19 studies, 1431 patients), the pooled node-based sensitivity and specificity were 0.68 and 0.96, respectively (1), and a similar pattern has been reported across institutional series (2, 3).

Attempts to improve diagnostic performance by refining the metabolic signal have been of limited value; in the multicentre MAPPING study, quantitative nodal thresholds did not outperform expert visual interpretation and were not recommended for routine use (4). From a clinical standpoint, a more relevant

question is where and why PET/CT errs. False-positive findings are largely a local nodal phenomenon, and reactive follicular hyperplasia is a recognised cause of benign FDG uptake (5). False-negative findings, in contrast, reflect small metastatic volume and the metabolic state at the time of imaging, since hyperglycaemia competitively reduces tumoural FDG uptake (6). These error patterns have rarely been examined on a station-by-station basis; in particular, the common iliac region is usually pooled into a single "pelvic" category and remains poorly characterised.

In the present study, using a two-centre cohort with histopathology as the gold standard, we report the diagnostic accuracy of FDG-PET/CT at each nodal station, identify where discordance with histopathology is concentrated, and test two pre-specified, clinically grounded hypotheses: that scan-day blood glucose is associated with false-negative findings, and that systemic inflammation is associated with false-positive findings.

Materials and Methods

Design, setting and participants

This retrospective, two-centre diagnostic accuracy study was reported in accordance with the Standards for Reporting of Diagnostic Accuracy (STARD) 2015 statement (18). Consecutive eligible women were identified from the gynecologic-oncology and nuclear-medicine records of two tertiary hospitals, designated Center 1 (İzmir Katip Çelebi University Atatürk Training and Research Hospital, İzmir) and Center 2 (University of Health Sciences, Gaziosmanpaşa Training and Research Hospital, İstanbul) and referred to as Center 1 and Center 2 throughout. Eligible patients had histologically confirmed endometrial, ovarian, cervical or vulvar cancer, had undergone preoperative FDG-PET/CT, and had proceeded to lymphadenectomy of one or more nodal stations. Patients who did not undergo lymphadenectomy were excluded, as histological verification would not be available. A nodal station was considered evaluable, and was included in the station-level analysis, only when it had been surgically removed and a histopathological result was available; stations that were not dissected provided no reference standard and were excluded rather than classified as negative. At each centre, all lymphadenectomies were performed by a single experienced gynecologic oncology surgeon, with a different surgeon at the two sites: at Center 2 by a professor of obstetrics and gynecology serving as clinical and surgical education director, with longstanding expertise in gynecologic-oncological and high-risk pelvic surgery (S.S.), and at Center 1 by an experienced gynecologic oncology surgeon performing the full spectrum of surgical staging procedures (S.Ş.). Both surgeons routinely performed systematic pelvic and para-aortic lymphadenectomy, so that surgical technique was consistent within each centre. As the operating surgeon coincided with the centre, the two were treated as a single factor in the analysis. Institutional ethics approval was obtained at each centre.

Index test and gold standard

At each centre, FDG-PET/CT was performed on a dedicated PET/CT scanner, with a different system used at the two sites (Center 1, GE Discovery 710; Center 2, Siemens Biograph), according to a routine clinical protocol broadly consistent with the EANM tumour-imaging procedure guidelines (19). Patients fasted before imaging (median 8 h), pre-injection blood glucose was recorded, and a weight-adjusted activity of ^{18}F-FDG was administered (median 322 MBq, range 180–450), followed by an uptake period of approximately 60 min (median 61 min, range 45–81). Images were acquired from the skull base to the mid-thigh, together with a low-dose CT for attenuation correction and anatomical localisation. PET data were reconstructed using an ordered-subset expectation-maximisation (OSEM) algorithm (matrix 200–256; Gaussian post-filter 4–6 mm full width at half maximum), and the low-dose attenuation-correction CT was acquired at 100–120 kVp with a reduced tube current. Station- and patient-level positivity was determined from the standard clinical PET/CT reports rather than from a separate blinded re-reading of the images: a node was regarded as positive when the report described focal uptake above local background, irrespective of size. Two readers (S.Ş. and F.G.Ş.) applied this classification independently, so that their agreement reflects the consistency of report-based study classification rather than primary image interpretation; the few discrepancies were subsequently resolved by consensus, including telephone consultation when required, to yield the final dataset. The most avid nodal SUVmax, the primary-tumour SUVmax and a hepatic reference SUVmax were recorded, and a nodal-to-liver SUVmax ratio was derived in order to limit cross-scanner variation. Histopathological examination of the surgical specimen served as the gold standard. Diagnostic accuracy was assessed at the level of the individual nodal station: a station was classified as histologically positive when it contained at least one metastatic node, and as PET-positive when FDG-PET/CT identified at least one suspicious node. Each patient contributed up to four stations (pelvic, para-aortic, common iliac [kept separate] and inguinal). As inguinal dissection is performed almost exclusively for vulvar disease, the inguinal station is reported descriptively.

Statistical analysis

Analyses were performed in Python 3 (NumPy and pandas). For each nodal station, sensitivity, specificity, positive and negative predictive values and accuracy were calculated against histopathology, each with Wilson 95% confidence intervals (20); for the overall estimates, patient-level cluster bootstrap confidence intervals were additionally computed to account for the clustering of stations within patients, together with positive and negative likelihood ratios. The two pre-specified determinant analyses (scan-day glucose versus false-negative findings, and the neutrophil-to-lymphocyte ratio versus false-positive findings) were performed using single-predictor logistic regression with robust (sandwich) standard errors clustered on the multiple stations within each patient, and were reported as odds ratios with 95% confidence intervals; the platelet-to-lymphocyte ratio and the systemic immune-inflammation index were tested as alternatives, with false-discovery-rate control. As a secondary, patient-level analysis, primary-tumour SUVmax, tumour size and grade were related to nodal metastasis using the Mann–Whitney U test and uni- and multivariable logistic regression (three predictors; ten events per variable), with receiver-operating-characteristic analysis for primary-tumour SUVmax (AUC, bootstrap 95% confidence

interval and Youden-optimal cut-off). Diagnostic accuracy was also examined within each centre and compared between endometrial and non-endometrial tumours. Agreement between the two readers on the patient-level PET classification was quantified using Cohen's κ with its 95% confidence interval. No a priori sample size was calculated for this fixed retrospective cohort; with 48 histologically positive and 232 histologically negative stations, sensitivity and specificity were estimated to within approximately 13 and 3 percentage points, respectively. Continuous variables are summarised as median (interquartile range); covariate data were essentially complete, and a two-sided p value < 0.05 was considered statistically significant.

Results

Patients

A total of 120 women were analysed (Center 1, 83; Center 2, 37; Fig. 1, Table 1). Endometrial carcinoma was the predominant tumour type (61%), and lymph node metastasis was present in 30 patients (25%). The two centres differed in case-mix: Center 1 comprised older patients, a higher proportion of ovarian cancers and a higher rate of lymph node metastasis. These between-centre differences are descriptive; as centre coincided with surgeon, scanner and era, they are not interpreted causally.

Table 1
Baseline characteristics, overall and by centre, with between-centre comparison.

Characteristic	Overall (n = 120)	Center 1 (n = 83)	Center 2 (n = 37)	p
Age, median (IQR), y	62 (54–69)	65 (56–72)	58 (51–62)	0.004
Tumour type, n				0.001
Endometrial	73 (61%)	41	32	
Ovarian	33 (28%)	28	5	
Cervical	8 (7%)	8	0	
Vulvar	6 (5%)	6	0	
FIGO I / II / III / IV	48 / 24 / 33 / 15	34 / 22 / 20 / 7	14 / 2 / 13 / 8	0.015
Grade 1 / 2 / 3	43 / 41 / 36	27 / 28 / 28	16 / 13 / 8	0.352
Tumour size, median (IQR), mm	39 (29–47)	38 (29–48)	39 (28–47)	0.952
PET-to-surgery interval, median (IQR), d	22 (14–28)	23 (16–29)	18 (13–26)	0.041
Fasting, median (IQR), h	7.6 (6.3–8.7)	7.6 (6.4–8.6)	7.4 (5.9–8.7)	0.547
Scan-day glucose, median (IQR), mg/dL	103 (90–113)	105 (95–116)	94 (87–108)	0.036
Haemoglobin, median (IQR), g/dL	12.6 (11.6–13.4)	12.6 (11.6–13.3)	12.8 (11.7–13.5)	0.477
NLR, median (IQR)	2.4 (1.6–3.4)	2.3 (1.7–3.4)	2.4 (1.6–3.3)	0.986
Lymph node metastasis, n (%)	30 (25%)	23 (28%)	7 (19%)	0.304

Data are median (interquartile range, IQR) or n (%). p values: Mann–Whitney U test for continuous variables and chi-square test for categorical variables, comparing Center 1 (İzmir) with Center 2 (İstanbul). NLR, neutrophil-to-lymphocyte ratio.

Lymphovascular space invasion was not reliably recorded and is therefore not reported. On formal comparison (Table 1), the two centres were comparable with respect to tumour size, fasting duration, haemoglobin and all inflammatory indices, including the neutrophil-to-lymphocyte ratio (p = 0.99), as well as the rate of lymph node metastasis (p = 0.30). They differed in patient age (p = 0.004), tumour-type distribution (p = 0.001), FIGO stage (p = 0.015), the PET-to-surgery interval (p = 0.04) and scan-day glucose (p = 0.04), reflecting differences in referral case-mix. The comparability of the inflammatory indices supports interpretation of the neutrophil-to-lymphocyte ratio analysis independently of centre; conversely, the modest between-centre difference in scan-day glucose represents a potential confounder for the glucose analysis and is addressed in the limitations.

Accuracy at each nodal station

Across 280 evaluable stations, FDG-PET/CT was highly specific but only moderately sensitive (overall sensitivity 62.5%, 95% CI 48–75; specificity 94.0%, 90–96; Table 2, Fig. 2). Sensitivity was highest at the pelvic station (71%) and lowest at the para-aortic station (45%). The common iliac station was notable for a low positive predictive value (27%), indicating that most positive findings at this station were not confirmed at pathology. The inguinal station was evaluable in only the six patients with vulvar cancer. After accounting for the clustering of stations within patients (patient-level bootstrap), the overall estimates were essentially unchanged (sensitivity 62.5%, 95% CI 49–75; specificity 94.0%, 90–97; positive predictive value 68%, 51–84; negative predictive value 92%, 88–96), corresponding to a positive likelihood ratio of 10.4 (95% CI 5.9–23.0) and a negative likelihood ratio of 0.40 (0.27–0.55). In the tumour-type-stratified analysis, station-level accuracy was similar in endometrial (sensitivity 62%, specificity 95%) and non-endometrial cancers (sensitivity 64%, specificity 93%; Table 3), indicating that pooling across tumour types did not materially distort the overall estimates; nonetheless, the cohort was predominantly endometrial (61%), and the findings apply chiefly to that setting. Agreement between the two readers' independent report-based classifications was high (observed agreement 93%; Cohen's κ = 0.81, 95% CI 0.68–0.94).

Table 2
Station-level diagnostic accuracy (Wilson 95% CI).

Station	N	TP	FP	FN	TN	Sensitivity	Specificity	PPV	NPV	Accuracy
Pelvic	103	20	4	8	71	71% (53–85)	95% (87–98)	83%	90%	88%
Para-aortic	65	5	2	6	52	45% (21–72)	96% (87–99)	71%	90%	88%
Common iliac	106	3	8	3	92	50% (19–81)	92% (85–96)	27%	97%	90%
Inguinal	6	2	0	1	3	67% (21–94)	100% (44–100)	100%	75%	83%
Overall	**280**	**30**	**14**	**18**	**218**	**62.5% (48–75)**	**94.0% (90–96)**	**68%**	**92%**	**89%**

Table 3
Station-level diagnostic accuracy by tumour type.

Group	Patients	Stations	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Endometrial	73	158	62% (43–78)	95% (89–97)	70% (49–84)	93% (87–96)
Non-endometrial	47	122	64% (43–80)	93% (86–97)	67% (45–83)	92% (85–96)
Overall	120	280	62.5% (48–75)	94% (90–96)	68% (53–80)	92% (88–95)

Wilson 95% confidence intervals. PPV, positive predictive value; NPV, negative predictive value.

Pattern of discordance with histopathology

Discordance with histopathology was asymmetric. Of 48 histologically positive stations, 18 (37.5%) were classified as PET-negative (false negatives), whereas of 232 histologically negative stations, only 14 (6.0%) were classified as PET-positive (false positives). False negatives were therefore the predominant error at every station except the common iliac, where false positives outnumbered false negatives (Fig. 3). At the patient level (prevalence 30/120), the sensitivity was 76.7% (95% CI 59–88), specificity 81.1% (72–88), positive predictive value 57.5%, negative predictive value 91.3% and accuracy 80.0%.

Scan-day glucose and inflammation

False-negative stations were associated with modestly higher scan-day blood glucose than true-positive stations (median 110 vs 102 mg/dL; odds ratio 1.30 per 10 mg/dL, 95% CI 0.91–1.86; p = 0.15). Although the direction was consistent, the association did not reach statistical significance. The neutrophil-to-lymphocyte ratio was not associated with false-positive findings (odds ratio 0.92, 95% CI 0.61–1.38; p = 0.68), and the platelet-to-lymphocyte ratio and the systemic immune-inflammation index yielded concordant results.

Predictors of nodal metastasis

At the patient level, a higher primary-tumour SUVmax was strongly associated with nodal metastasis (median 16.2 vs 11.2), with an area under the curve of 0.73 (95% CI 0.62–0.83); the Youden-optimal cut-off of 13.7 yielded a sensitivity of 77% and a specificity of 63% for nodal involvement (Fig. 4). Larger tumour size and higher grade (node-positive rates of 9%, 29% and 39% for grades 1, 2 and 3, respectively) were also associated with nodal metastasis, whereas age, scan-day glucose and the neutrophil-to-lymphocyte ratio were not. In the multivariable model, all three predictors remained independently associated with nodal metastasis (Table 4). By contrast, neither the recorded nodal

SUVmax nor the derived nodal-to-liver SUVmax ratio could be evaluated as an independent quantitative index, because in this dataset they were available only for histologically positive stations and were therefore not analysable against the reference standard.

Table 4
Predictors of lymph node metastasis (univariable and multivariable logistic regression).

Predictor	Univariable OR (95% CI)	p	Adjusted OR (95% CI)	p
Primary-tumour SUVmax (per + 5 units)	2.22 (1.45–3.40)	< 0.001	2.00 (1.26–3.18)	0.003
Tumour size (per + 10 mm)	1.52 (1.11–2.06)	0.008	1.53 (1.07–2.20)	0.02
Tumour grade (per grade)	2.32 (1.33–4.04)	0.003	2.43 (1.28–4.64)	0.007

Logistic regression (n = 120; 30 with nodal metastasis). The adjusted model includes all three predictors simultaneously. OR, odds ratio; CI, confidence interval.

Discussion

The principal clinical message of this two-centre series is straightforward: when FDG-PET/CT reports a node as positive, the finding is usually correct, whereas a negative report frequently fails to exclude disease. Specificity was 94% and most positive findings were confirmed at histopathology, yet more than one-third of histologically positive stations were classified as PET-negative. This is the well-recognised diagnostic behaviour of PET, namely high specificity with limited sensitivity (1, 2), and it is the most important consideration for surgical decision-making.

This diagnostic asymmetry has direct implications for surgical staging. A negative nodal FDG-PET/CT result should not, in itself, justify omitting lymphadenectomy or sentinel-lymph-node mapping when lymph node involvement would alter adjuvant treatment. The metastases missed by PET were predominantly low-volume, and PET is known to overlook the micrometastatic and low-volume deposits detected by sentinel-lymph-node biopsy with ultrastaging; it cannot replace surgical lymph node staging for this purpose (8). In endometrial cancer in particular, sentinel-lymph-node biopsy with ultrastaging achieves a sensitivity of approximately 97% and a negative predictive value approaching 100%, and is now endorsed as an alternative to systematic lymphadenectomy in current guidelines and consensus statements (9, 10, 14, 16); this represents a level of nodal detection that PET cannot approach, and underscores that imaging should complement rather than replace surgical nodal assessment when staging will alter treatment. PET/CT is therefore better suited to confirming suspected nodal or distant disease and to directing biopsy than to excluding lymph node involvement. Our patient-level sensitivity of 77% is broadly consistent with prospective multicentre data in high-risk endometrial cancer (7) and reinforces the same caution.

The station-specific pattern is also in keeping with disease-specific experience. The low para-aortic sensitivity observed in our cohort (45%) parallels reports that FDG-PET/CT misses para-aortic metastasis in a clinically meaningful proportion of women with locally advanced cervical cancer, even with modern time-of-flight systems (11); this is the rationale for which surgical para-aortic staging is still undertaken when it would modify the radiation field, in line with current guidelines (15). Comparative imaging studies have similarly shown that PET/CT performs comparably to magnetic resonance imaging for nodal staging in endometrial cancer, with neither modality being sufficiently sensitive to exclude nodal disease (12). Our findings extend these observations by localising, within a single cohort, where the diagnostic shortfall is greatest.

Analysis on a station-by-station basis drew particular attention to the common iliac region, where only approximately one in four positive findings was confirmed at histopathology (positive predictive value 27%). This was the only station at which false-positive findings exceeded false-negative findings. Although the numbers were small, the pattern is consistent with the local anatomy: at the common iliac station, physiological ureteric and vascular activity and benign reactive (follicular) hyperplasia, a recognised cause of false-positive nodal FDG uptake (5), may readily be mistaken for metastasis. In clinical practice, an isolated FDG-avid common iliac node warrants correlation with the CT component and, where it would alter the extent of surgery, histological confirmation rather than acceptance as metastatic. Reporting this station within a single "pelvic" category, as is common practice, conceals precisely this pitfall and argues for reporting it separately in routine practice.

A potentially modifiable factor also emerged. False-negative stations tended to occur on scans performed at higher blood glucose, consistent with a large pooled analysis demonstrating that elevated blood glucose significantly reduces lesional FDG uptake through competitive inhibition (6). In our data, this represented a non-significant trend rather than a definitive finding and requires prospective confirmation; it is in keeping with standard scan preparation, in that adequate fasting and normoglycaemia before FDG-PET/CT are already routine, and it serves, at most, as a reminder that lapses may reduce sensitivity. By contrast, no association was found between the neutrophil-to-lymphocyte ratio and false-positive findings, suggesting that benign FDG-avid nodes arise from local nodal biology rather than from the systemic inflammatory state of the patient; systemic inflammatory indices are therefore unlikely to assist in discriminating reactive from malignant uptake.

A complementary observation reinforces the central message. Although the nodal sensitivity of PET is limited, the metabolic activity of the primary tumour itself carried independent information: a higher primary-tumour SUVmax predicted nodal metastasis with moderate discrimination (AUC 0.73) and remained independent after adjustment for tumour size and grade, consistent with reports that metabolic primary-tumour markers predict nodal metastasis in endometrial cancer (17). Clinically, this implies that in a woman with a highly FDG-avid, large or high-grade primary tumour, a negative nodal PET should be interpreted with particular caution, as the pre-test probability of occult nodal disease is high; such patients are precisely those in whom surgical nodal assessment remains most valuable. This

finding should be regarded as hypothesis-supporting rather than as a validated tool, given the moderate discrimination and the single retrospective cohort.

This study has several limitations. It is retrospective and confined to two tertiary hospitals; because centre coincided with the operating surgeon, the scanner (GE Discovery 710 at Center 1 and Siemens Biograph at Center 2) and the recruitment era, these factors are confounded, and the differences between the two cohorts are descriptive only and do not constitute evidence of a "centre" effect. Importantly, only patients who proceeded to lymphadenectomy were included, as histology was required as the gold standard; the accuracy estimates therefore pertain to a surgically selected population, are subject to verification (work-up) bias, and need not apply to all patients undergoing PET. The two exploratory associations were based on few events (18 false-negative and 14 false-positive stations), were each restricted to a single, unadjusted predictor and are hypothesis-generating only; in particular, the association between higher scan-day glucose and false-negative findings is unadjusted and may be confounded by tumour type, the PET-to-surgery interval and centre, given that scan-day glucose differed between the two centres. The analysis was performed at the level of the nodal station rather than the individual node, as node-to-node matching with imaging is not feasible; the inguinal station was evaluable in only six patients with vulvar cancer; lymphovascular space invasion was not reliably recorded; and the scans were classified from the clinical reports by two study readers rather than by a separate blinded image re-reading or by readers external to the study, although their independent report-based classifications showed good agreement ($\kappa = 0.81$). Finally, the cohort was drawn from a single country and from public tertiary centres, which may limit generalisability.

In summary, PET-based lymph node staging in gynecologic cancer is most useful when its asymmetry is borne in mind: a positive finding may be acted upon, a negative finding does not exclude metastasis, the common iliac station warrants particular caution, and scan-day glucose showed only a non-significant trend towards a higher rate of false-negative findings. The high reliability of a positive read is of immediate practical value, whereas the glucose and common iliac signals are hypothesis-generating and require confirmation in larger prospective studies.

Abbreviations

CI
confidence interval
FDG
fluorodeoxyglucose
FIGO
International Federation of Gynecology and Obstetrics
NLR
neutrophil-to-lymphocyte ratio
NPV
negative predictive value

PET/CT
positron emission tomography/computed tomography
PPV
positive predictive value
SLN
sentinel lymph node
STARD
Standards for Reporting of Diagnostic Accuracy
SUVmax
maximum standardized uptake value.

Declarations

Ethics approval. The study was approved by the Clinical Research Ethics Committee of İzmir Katip Çelebi University Atatürk Training and Research Hospital (decision no. 0191, dated 15 April 2021) and by the institutional ethics committee of the University of Health Sciences, Gaziosmanpaşa Training and Research Hospital, İstanbul. The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate. Owing to the retrospective design, the requirement for individual informed consent was waived by the ethics committees.

Prior data use. Part of the Center 1 cohort was collected under a previously approved institutional data-collection protocol; the present two-centre study is a new, combined analysis that has not been published or submitted elsewhere.

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Conflicts of interest. The authors declare no competing interests.

Author contributions. Concept and design: F.G.Ş., S.Ş., S.S. Surgery and clinical data acquisition: S.Ş. (İzmir centre), S.S. (İstanbul centre), F.İ., H.B.B., F.K.G. Data curation: F.G.Ş., F.İ., H.B.B., F.K.G. Statistical analysis and interpretation: S.Ş., F.G.Ş. Drafting: S.Ş., F.G.Ş. Study supervision: S.A. Critical revision for important intellectual content: all authors. All authors read and approved the final manuscript.

Use of artificial intelligence. The authors used a large language model–based assistant (Claude, Anthropic) for language editing, drafting support, preparation of figures and statistical code. The tool was not used for autonomous generation of content; all data analyses, interpretations and the final manuscript were reviewed, verified and approved by the authors, who take full responsibility for the integrity and content of the work. No artificial-intelligence tool meets authorship criteria or is listed as an author.

Data availability. De-identified data are available from the corresponding author on reasonable request.

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Figures

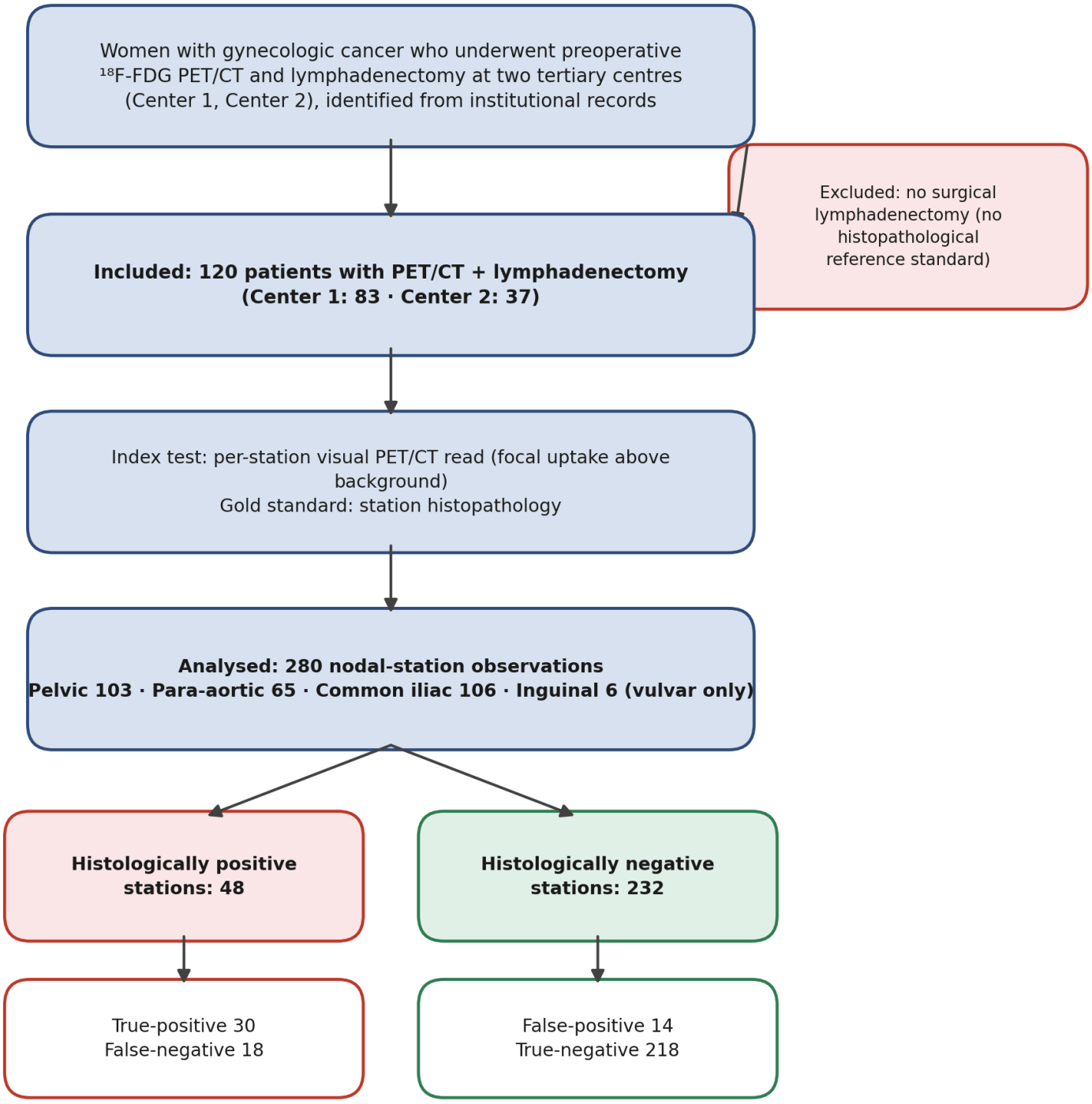


Figure 1

STARD 2015 patient-and-station flow (locked two-centre dataset).

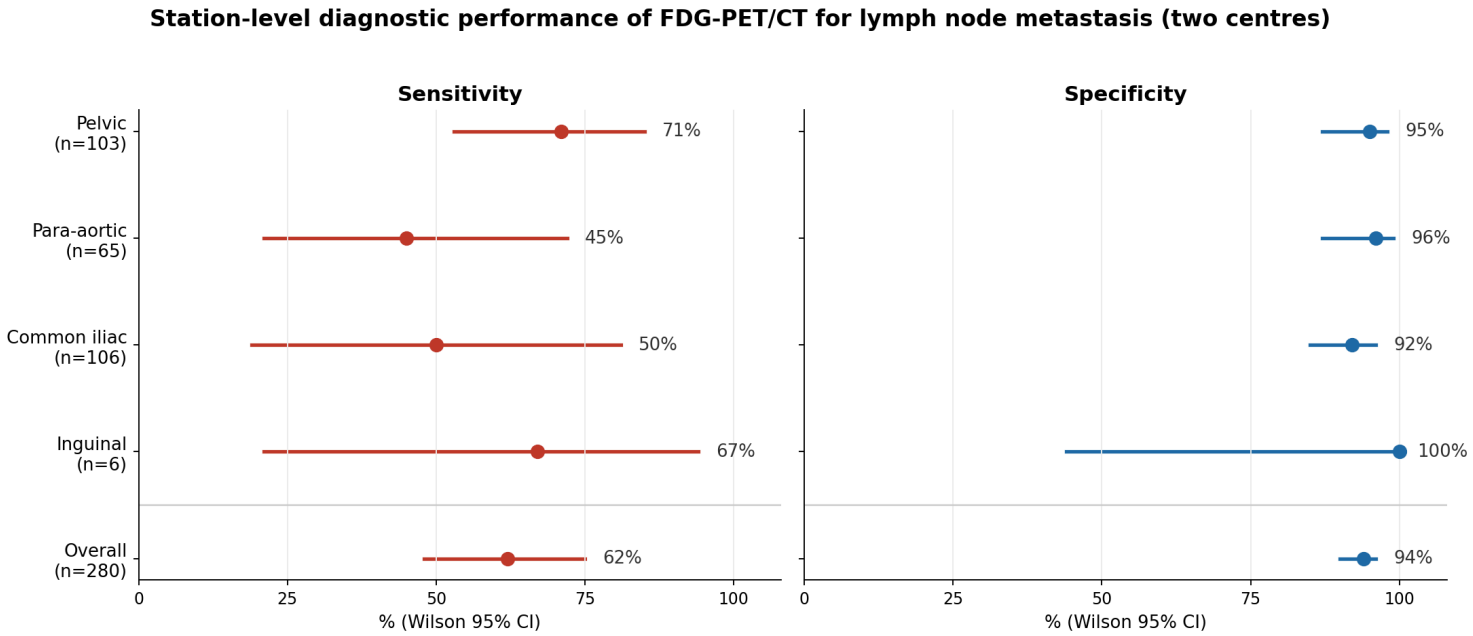


Figure 2

Station-level sensitivity and specificity with Wilson 95% confidence intervals.

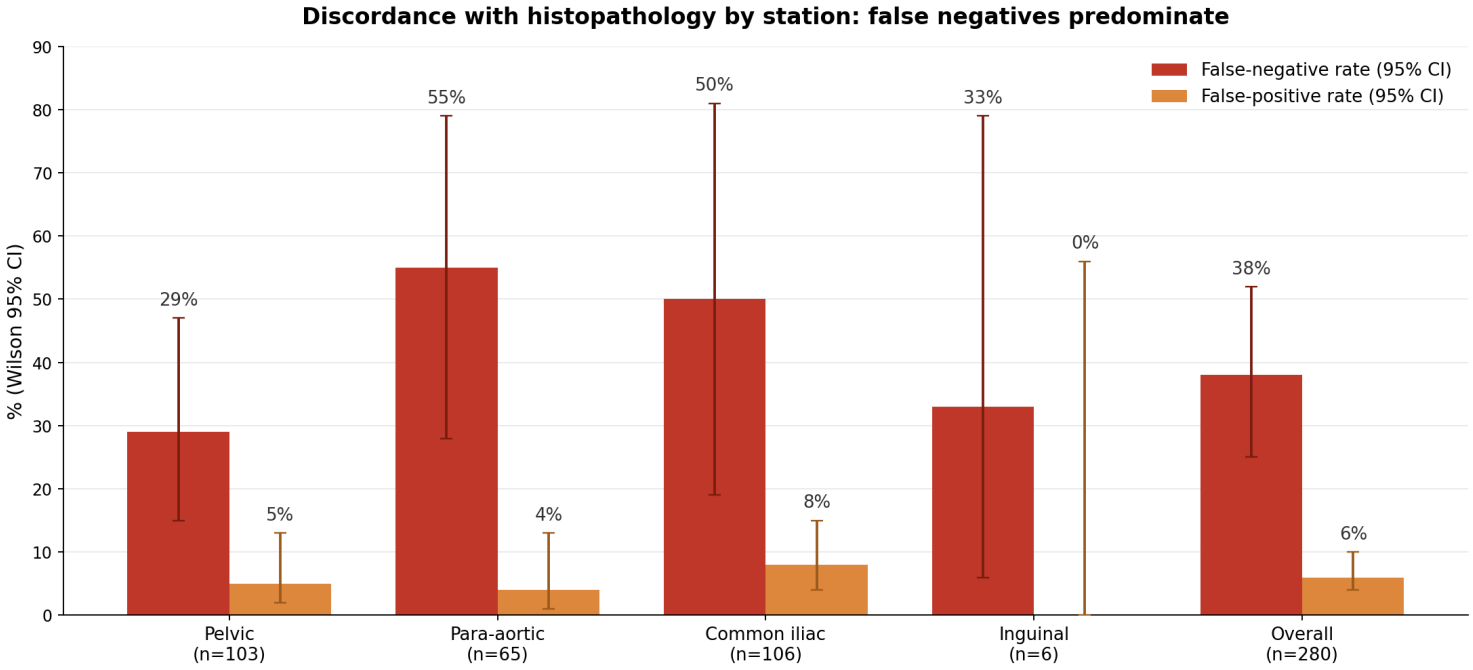


Figure 3

False-negative versus false-positive rates by station.

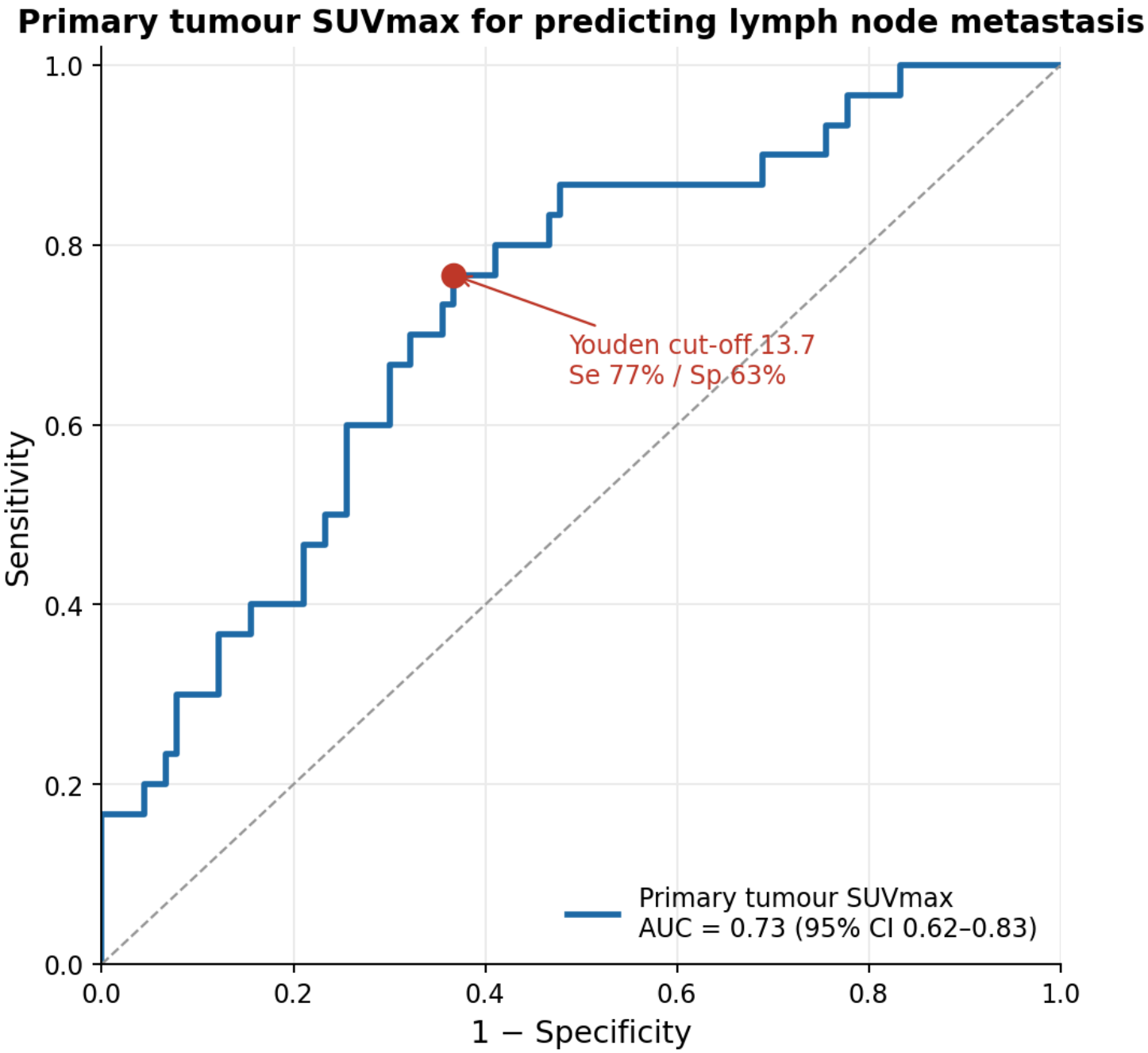


Figure 4

Receiver-operating-characteristic curve of primary-tumour SUVmax for predicting lymph node metastasis.