Risk Factors for Positive Deep Pelvic Nodal Involvement in Patients with Palpable Groin Melanoma Metastases: Can the Extent of Surgery Safely Be Minimized? *A Retrospective Multicenter Cohort Study*

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Abstract

Background Patients with palpable melanoma groin metastases have a poor prognosis. There is debate whether a combined superficial (SGD) and deep groin dissection (CGD) is necessary or if SGD alone is sufficient. This study analyses risk factors for deep pelvic nodal involvement.

Methods This retrospective multicenter cohort study concerned 209 therapeutic CGDs from four tertiary centers in the Netherlands (1992–2013), selected based on complete preoperative imaging and pathology reports. Analyzed risk factors included baseline and primary tumor characteristics, total and positive number of inguinal nodes, inguinal lymph node ratio (LNR) and positive deep pelvic nodes on imaging (CT ± PET, or PET - low dose CT).

Results Median age was 57 years, 54% was female, median follow-up was 21 months (inter quartile range (IQR) 11-46 months). Median Breslow thickness was 2.10mm (IQR 1.40-3.40mm), 26% was ulcerated. Positive deep pelvic nodes occurred in 35% of CGDs. Significantly fewer inguinal nodes were positive in case of negative deep pelvic nodes; median 1 (IQR 1-2) versus 3 (IQR 1-4) for positive deep pelvic nodes ($p<0.001$). LNR was significantly lower for negative versus positive deep pelvic nodes; median 0.15 (IQR 0.10-0.25), versus 0.33 (IQR 0.14-0.54) ($p <0.001$). Combination of negative imaging, low LNR, low number of positive inguinal nodes and no extracapsular extension could accurately predict absence of pelvic nodal involvement in 84%.

Conclusion Patients with negative imaging, few positive inguinal nodes, no extracapsular extension and low LNR, have low risk of positive deep pelvic nodes and may safely undergo SGD alone.

Introduction

Patients with clinically palpable nodal metastases of cutaneous melanoma in the groin have a poor prognosis. Balch et al. reported a 5-year overall survival (OS) rate of 59% for stage IIIB melanoma in the 2009 AJCC melanoma staging system analysis[1]. Reported 5-year OS rates for the subgroup of patients with palpable groin metastases range from 52% for superficial involvement to 12% for deep involvement[2-7].

Standard of care for these patients consists of therapeutic lymph node dissection (TLND)[2, 8-10]. There is ongoing debate, whether this should consist of either a combined superficial and deep groin dissection (CGD) or that merely a superficial groin dissection (SGD) would suffice.

Several cohort studies seem to indicate no difference in survival between these two procedures, and patients may benefit from SGD alone if no positive deep pelvic nodes are present on preoperative imaging [2, 8, 10-12].

Since the estimated prevalence of positive deep pelvic nodes in patients with palpable inguinal lymph nodes is 30%, the majority of patients undergoing CGD may not benefit from deep groin dissection (DGD)[6, 12]. As CGD is a more extensive procedure than SGD, the risk of morbidity is potentially higher[6]. A clear need exists to select those patients who can be safely spared a DGD in absence of deep pelvic nodal involvement[10, 11, 13-15].

Preoperative imaging techniques such as CT and positron emission tomography (PET) form a valuable adjunct to staging. Up to 27% of patients presenting with palpable lymph node metastases have synchronous distant metastases at preoperative PET/CT, which changes the indication for surgery into palliative resection and/or systemic therapy[16]. Additionally, imaging provides assessment of suspicious deep pelvic nodes prior to surgery. High positive (PPV) and negative predictive value (NPV) have been achieved by Allan et al, (100% and 86% respectively)[3]. Other series reported PPV and NPV of 40-60%, which is too low to confirm or reject presence of positive deep pelvic nodes based on preoperative imaging alone[2, 17, 18]. Once suspicious deep pelvic nodes are detected on preoperative imaging, one cannot ignore their presence, and CGD is highly recommended. Absence of suspicious deep pelvic nodes on imaging does not rule out deep pelvic nodal involvement. Once imaging has been performed the focus should be on identification of further risk factors for positive deep pelvic nodes[2, 7, 11, 15, 17-21].

Aim: to analyze risk factors for deep pelvic nodal involvement in a retrospective multicenter cohort of palpable groin melanoma metastases. This could aid in the development of an algorithm for selective surgery in the future.

Patients and Methods

Patients

This retrospective multicenter cohort study describes 209 therapeutic CGDs performed at four tertiary melanoma centers in the Netherlands between 1992 and 2013. Patient selection was based on presence of a palpable nodal metastasis to the groin, complete pathology reports of the performed CGD, (i.e. clearly describing the dissected lymph nodes as inguinal or iliac, including obturator area), and preoperative imaging (CT, PET or PET/CT). Patients without imaging, with prior lymph node dissections in the groin area or with isolated limb perfusion or positive sentinel node(s) as indication for CGD were excluded. Analyzed preoperative imaging modalities were: CT scan, PET, and combined PET with low dose CT (PET-CT).

All patient characteristics were obtained from medical records and collected in a database for the current retrospective multicenter cohort study, according to local institutional review committee guidelines and national legislation.

Surgical Procedure

CGD was performed either via two separate transverse incisions, or via an inguinal ellipse shaped incision extending cranially according to local preferences per center, as described in detail elsewhere[6, 22].

Pathology

CGD pathology reports were considered adequate when clear description was given of the total number of inguinal nodes, as well as the number of tumor positive inguinal nodes, and similar description was given of the number of dissected deep pelvic nodes (iliac nodes and obturator nodes) and the number of tumor positive deep pelvic nodes.

Statistics / Data analysis

Patients were divided into two categories based on deep pelvic nodal status: positive or negative. Univariable Chi-squared tests were performed to test for significant differences in prevalence of gender, primary tumor located on the trunk, primary tumor stage (T1-T4), ulceration, and inguinal extracapsular extension (ECE). Nonparametric tests were performed to test for differences in age, median Breslow thickness, total number of inguinal nodes and number of positive inguinal nodes, total number of excised nodes and number of positive nodes, total number of deep pelvic nodes, number of positive deep pelvic nodes, and LNR. Sensitivity, specificity, PPV, NPV, and accuracy were calculated for all imaging modalities using number of true positives (TP), false positives (FP), true negatives (TN) and false negatives (FN).

Differences in baseline characteristics were tested with univariable logistic regression analysis. Multivariable models were calculated using variables significant at univariable

analysis. Binary logistic multivariable regression analyses were performed to test for independent predictors of deep pelvic nodal involvement.

Ridge regression analysis was performed to exclude the influence of multicollinearity in a prediction model based on independent predictive variables. An area under the receiver operating characteristic curve (AUC) was calculated for the model. The AUC indicates the probability that patients with observed positive deep pelvic nodes had a higher predicted probability than patients with observed negative deep pelvic nodes, providing information about the predictive value of the model.

All statistical analyses except Ridge regression were performed using SPSS Version 21.0 (IBM Corp. Released 2012. Armonk, NY, United States). Ridge regression was performed using RStudio (RStudio Inc. Boston, Massachusetts, United States). An $\alpha < 0.05$ was considered significant.

Results

Patients

Table 1 gives an overview of baseline characteristics. The majority of patients (n=201, 96%) had palpable stage IIIB disease, eight patients (4%) had stage IV disease. Median Breslow thickness was 2.10 mm (IQR 1.4 - 3.4 mm). Twelve patients had a history of negative sentinel node. Median follow-up was 21 months (IQR 11 - 46 months).

Imaging and Pathology

Four patients underwent both CT and PET/CT, they were scored as PET/CT since the additional information obtained from PET/CT was used for final determination of clinical nodal status. Predictive accuracy per imaging modality is shown in **table 2**. The different imaging modalities were used equally between the two groups (i.e. positive or negative deep pelvic nodes).

Logistic regression analysis

Variables significantly different on univariable analysis (**table 1**) were included in multivariable binary logistic regression analyses. LNR and number of positive inguinal lymph nodes were assessed in separate models due to evident multicollinearity. Remaining significant independent predictors were: suspicious deep pelvic nodes on imaging (odds ratio (OR) 9.64, 95% CI 4.35 – 21.3, $p < 0.001$), increasing LNR (OR 34.2, 95% CI 5.47 – 214, $p < 0.001$), presence of ECE (OR 2.13, 95% CI 1.01 – 4.48, $p = 0.046$), and in a separate multivariable model without LNR: increasing number of positive inguinal lymph nodes (OR 1.27, 95% CI 1.06 – 1.53, $p = 0.010$).

Table 1. Baseline Characteristics.

Characteristic	*Total n=209 (100%)*	*Pelvic Nodes - n=135 (65%)*	*Pelvic Nodes + n=74 (35%)*	*P*
	n,(%)	*n, (%)*	*n, (%)*	
Gender				
Female	114 (54)	76 (56)	38 (51)	
Male	95 (46)	59 (44)	36 (49)	0.49
Age (yrs) median (IQR)	57 (45 - 65)	55 (46 - 65)	59 (44 - 65)	0.63
Center				
1	60 (29)	42 (31)	18 (24)	
2	57 (27)	38 (28)	19 (26)	
3	24 (12)	11 (8)	13 (18)	
4	68 (32)	44 (33)	24 (32)	0.21
Tumor stage				
T1	22 (11)	9 (7)	13 (18)	
T2	57 (27)	36 (27)	21 (28)	
T3	60 (29)	39 (29)	21 (28)	
T4	30 (14)	22 (16)	8 (11)	
Unknown primary	10 (5)	8 (6)	2 (3)	
Missing	30 (14)	21 (15)	9 (12)	0.16
Ulceration				
Absent	125 (60)	74 (55)	51 (69)	
Present	54 (26)	38 (28)	16 (22)	
Missing	30 (14)	23 (17)	7 (9)	0.16
Clark level**				
II	1 (0.5)	0 (-)	1 (1)	
III	35 (17)	22 (16)	13 (17)	
IV	84 (40)	54 (40)	30 (41)	
V	13 (6)	11 (8)	2 (3)	
Missing	76 (36.5)	48 (36)	28 (38)	0.29
Location				
Leg	166 (80)	106 (79)	60 (81)	
Trunk	28 (13)	17 (13)	11 (15)	
Unknown primary	10 (5)	8 (6)	2 (3)	
Missing	5 (2)	4 (3)	1 (1)	0.62
Histology				
SSM	67 (32)	44 (32)	23 (31)	
NM	37 (18)	28 (21)	9 (12)	
Other	15 (7)	9 (7)	6 (8)	
Unknown primary	10 (5)	8 (6)	2 (3)	
Missing	80 (38)	46 (34)	34 (46)	0.24

Table 1. Baseline Characteristics. (continued)

Characteristic	*Total n=209 (100%)*	*Pelvic Nodes - n=135 (65%)*	*Pelvic Nodes + n=74 (35%)*	*P*
	n,(%)	*n, (%)*	*n, (%)*	
№ nodes, median (IQR)				
Inguinal	10 (7 - 13)	10 (7 - 13)	9 (7 - 12)	0.54
Deep	6 (4 - 10)	6 (4 - 9)	8 (5 - 11)	0.039*
Total	17 (13 - 22)	17 (13 - 21)	17 (14 - 22)	0.39
№ positive nodes, median (IQR)				
Inguinal	2 (1 - 3)	1 (1 - 2)	3 (1 - 4)	<0.001*
Deep	0 (0 - 1)	0 (0)	2 (1 - 3)	<0.001*
Total	2 (1 - 4)	1 (1 - 2)	5 (3 - 7)	<0.001*
LNR				
median (IQR)	0.20 (0.11 - 0.33)	0.15 (0.10 - 0.25)	0.33 (0.14 - 0.54)	<0.001*
Inguinal ECE				
No	134 (64)	94 (70)	40 (54)	
Yes	75 (36)	41 (30)	34 (46)	0.025*

n, number of patients; P, p-value; yrs, years; IQR, inter quartile range; T1, Breslow <1.00mm; T2, Breslow 1.01-2.00mm; T3, Breslow 2.01-4.00mm; T4, Breslow >4.00mm; №, number of; LNR, inguinal lymph node ratio; ECE, extracapsular extension.
**significant, p<0.05. Calculated with Chi-square and non-parametric tests ** Clark level II and III were combined for Chi-Square test.*

Table 2. Identification of Positive Deep Pelvic Lymph Nodes Using Preoperative Imaging Techniques (n=209).

	CT (n=67)	CT and/ or PET (n=57*)	PET/CT (n=85**)
Sensitivity	57%	36%	61%
Specificity	93%	94%	83%
PPV	80%	73%	68%
NPV	83%	70%	79%
Accuracy	82%	70%	75%

Abbreviations: CT, computed tomography; PET, position emission tomography; PET/CT, combined PET and low dose CT; PPV, positive predictive value; NPV, negative predictive value.*; 13 patients underwent PET alone. **, 4 patients underwent separate CT as well.

Subgroup analysis negative imaging

Suspicious deep pelvic nodes on imaging were highly predictive for positive deep pelvic nodes. A subgroup of 155 patients without suspicious deep pelvic nodes on imaging was selected for further analysis of additional risk factors for positive deep pelvic nodes. Thirty-five of these patients (23%) had positive deep pelvic nodes at histopathological examination with H&E staining, i.e. imaging was false negative. Univariable analysis results are displayed in **table 3**. Multivariable analysis was performed including all

Table 3. Baseline Characteristics for patients with negative preoperative imaging.

Characteristic	Total (n=155)	Pelvic nodes – (n= 120)	Pelvic nodes + (n= 35)	P
	n (%)	n (%)	n (%)	
Gender				
Female	83 (54)	67 (56)	16 (46)	
Male	72 (46)	53 (44)	19 (54)	0.29
Age (yrs) median (IQR)	56 (45 - 64)	55 (46 - 65)	57 (44 - 64)	0.99
Center				
1	44 (28)	38 (32)	6 (17)	
2	48 (31)	35 (29)	13 (37)	
3	18 (12)	10 (8)	8 (23)	
4	45 (29)	37 (31)	8 (23)	0.17
Breslow median (IQR)	2.10 (1.40 - 3.25)	2.20 (1.45 - 3.55)	1.90 (1.15 - 2.80)	0.11
Tumor stage				
T1	14 (9)	8 (7)	6 (17)	
T2	45 (29)	33 (28)	12 (34)	
T3	44 (28)	37 (31)	7 (20)	
T4	23 (15)	19 (16)	4 (11)	
Unknown primary	9 (6)	7 (6)	2 (6)	
Missing	20 (13)	16 (13)	4 (11)	0.38
Ulceration				
Absent	90 (58)	67 (56)	23 (66)	
Present	44 (28)	36 (31)	8 (23)	
Missing	21 (14)	17 (13)	4 (11)	0.34
Clark level**				
II	1 (0.6)	0 (-)	1 (3)	
III	25 (16)	20 (17)	5 (14)	
IV	65 (42)	49 (41)	16 (46)	
V	11 (7)	11 (9)	0 (-)	
Missing	53 (34)	40 (33)	13 (37)	0.070
Location				
Leg	118 (76)	93 (78)	25 (71)	
Trunk	23 (15)	16 (13)	7 (20)	
Unknown primary	9 (6)	7 (6)	2 (6)	
Missing	5 (3)	4 (3)	1 (3)	0.81
Histology				
SSM	52 (34)	40 (33)	5 (14)	
NM	31 (20)	26 (22)	12 (34)	
Other	10 (6)	8 (7)	2 (6)	
Unknown primary	9 (6)	7 (6)	2 (6)	

Table 3. Baseline Characteristics for patients with negative preoperative imaging. (continued)

Characteristic	Total (n=155)	Pelvic nodes – (n= 120)	Pelvic nodes + (n= 35)	P
	n (%)	n (%)	n (%)	
Missing	53 (34)	39 (32)	14 (40)	0.86
Nº nodes, median (IQR)				
Total	17 (13 - 21)	17 (13 - 21)	17 (14 - 22)	0.42
Inguinal	10 (8 - 12)	10 (8 - 13)	9 (8 - 12)	0.69
Deep	6 (4 - 9)	6 (4 - 9)	7 (4 - 11)	0.15
Nº positive nodes, median (IQR)				
Total	2 (1 - 4)	1 (1 - 2)	5 (3 - 6)	<0.001*
Inguinal	1 (1 - 3)	1 (1 - 2)	3 (1 - 4)	<0.001*
Deep	0 (0)	0 (0)	2 (1 - 2)	<0.001*
LNR, median (IQR)	0.17 (0.11 - 0.31)	0.21 (0.10 - 0.25)	0.33 (0.13 - 0.50)	0.001*
ECE inguinal				
No	96 (62)	79 (66)	17 (49)	
Yes	59 (38)	41 (34)	18 (51)	0.075

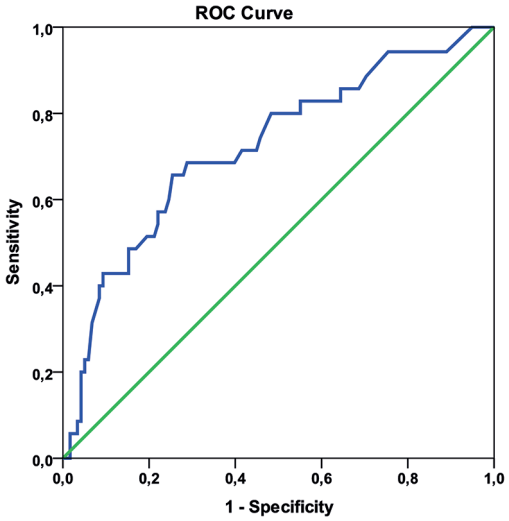
n, number of patients; P, p-value; ; yrs, years; IQR, inter quartile range; T1, Breslow <1.00mm; T2, Breslow 1.01-2.00mm; T3, Breslow 2.01-4.00mm; T4, Breslow >4.00mm; Nº, number of; LNR, inguinal lymph node ratio; ECE, extracapsular extension.

*, significant (p<0.05) ** for Chi-Square test Clark II & III were combined

significant variables assumed to be predictive for deep pelvic nodal status; number of positive inguinal nodes, LNR and ECE status. Evident multicollinearity was observed.

To overcome this problem a predictive Ridge logistic regression analysis was performed. Only LNR remained as significant independent predictor for positive deep pelvic nodes (p = 0.014). Number of positive inguinal lymph nodes and ECE were chosen to remain in the model as contributing covariates as these were thought to be of substantial additional clinical relevance. A receiver operating characteristic (ROC) curve of the predicted probabilities for positive deep pelvic nodes was created, displaying a fair AUC of 0.72 (AUC values range between 0 and 1, where high scores are indicative of high accuracy) (**Figure 1**).

The optimum cut-off value for the predicted probability of the model (i.e. the probability at which the model outcome correctly identifies an observed positive patient as positive) was chosen based on high specificity, in order to minimize false negative outcomes. Corresponding probability cut-off value and sensitivity were deduced from the ROC curve. For a specificity of 90%, the cut-off value for a positive test outcome was a probability for positive deep pelvic nodes of 32% or more. Sensitivity was 43%, PPV was 50%, NPV 84%, and overall accuracy of this model was 77%.



Area Under the Curve

Test Result Variable: Probability Deep Positive Nodes

AUC	SE[a]	Asymptotic Sig.[b]	Asymptotic 95% CI Lower Bound	Asymptotic 95% CI Upper Bound
,722	,051	,000	,622	,821

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5
AUC, area under the curve; SE, standard error; Sig., significance; 95% CI, 95% confidence interval.

Figure 1. ROC curve for prediction model probability positive deep nodes.
ROC; receiver operator characteristics.

Discussion

In this CGD cohort 35% of all patients have deep pelvic nodal involvement, which is in line with the literature[10, 11, 13-15]. This study analyses risk factors to identify deep pelvic nodal involvement. Imaging is a strong predictor. Our prediction model might lower the rate of CGD without positive pelvic nodes and minimizes the number of false negative outcomes after imaging.

Imaging

The imaging modalities used in this study are fair in correctly predicting positive deep pelvic nodes. Still a considerable number of patients have false positive imaging (20-32%). We can only speculate on the possible causes of false positive imaging. This might be partially explained by a small group of patients undergoing diagnostic excision biopsy of the palpable lymph node prior to imaging. This might cause a lymph node enlargement in the pelvic area. Another cause may be the inevitable interobserver vari-

ability in radiology. Improvement of imaging techniques over time may have altered the number of false positive lymph nodes detected during the present study period.

NPVs of the preoperative imaging techniques performed in the current study range between 70% and 83%, leaving a substantial proportion of 23% (17-30%) of patients to be falsely diagnosed with negative deep pelvic nodes. Several studies have reported on NPV of CT, and although high NPVs have been described by Allan et al, and Van der Ploeg et al., overall reported values range considerably [2, 3, 6, 17, 18]. Ongoing development of the newest imaging techniques such as use of a melanoma specific PET tracer ([18F] ICF01006) may enhance the accuracy of imaging and subsequently decrease the FN rate[23].

Predictive factors

Predictive factors for deep pelvic nodal involvement found in the current study are inguinal nodal status as defined by the number of positive inguinal nodes and LNR, inguinal ECE, and suspicious deep pelvic nodes on preoperative imaging, which is concordant with the literature [2, 7, 11, 15, 17-21]. These risk factors may be applied to select patients for SGD in addition to imaging without suspicious deep pelvic nodes. A hypothetical two stage approach would be: when preoperative imaging is negative, patients first undergo solely an SGD. The pathology results can then be used to determine the risk of occult positive deep pelvic nodes, and a decision can be made on whether to perform an additional DGD or not. The fact that patients must undergo two separate operations is a drawback, but this way, a DGD can be spared in 126 out of all patients (60%).

Patient Selection

Standard CGD for palpable stage III melanoma shows that 135 out of 209 deep pelvic groin dissections (65%) have been performed in the absence of pelvic nodal metastases.

Use of pre-operative imaging alone for selection between CGD and SGD would reduce the number of CGDs from 209 to 54. The remaining 155 patients would undergo SGD alone. Thirty-five of these 155 patients undergoing SGD alone are false negative (FN rate 23%), and would be possibly undertreated (i.e. undergoing no DGD).

Better patient selection is necessary in the negative imaging group, as potential decrease in the number of false negatives will make patient selection safer. This formed the rationale for the prediction model, which is based on 153 patients* (155 - 2 patients, *missing data) with negative imaging. Using this model 124 out of 153 patients would undergo SGD alone, and FN rates would be reduced to 20 out of 124 patients (FN rate 16%).

Concluding, this model forms an adjunct to the use of preoperative imaging as selection tool for SGD or CGD, both drastically minimizing the number of patients without

affected pelvic nodes undergoing a DGD, and controlling the number of patients with affected pelvic nodes potentially being undertreated by not undergoing a DGD.

The 16% FN rate of this model is still considerable. Although surgery forms the cornerstone of melanoma treatment, one may question the role of DGD in the current era of upcoming effective systemic treatments. On one hand, the majority of patients undergoing standard CGD for palpable groin metastases have negative deep pelvic nodes. On the other hand, there is evidence to assume that positive deep pelvic nodes may merely be a biomarker for stage IV disease, as survival rates depend on deep pelvic nodal status rather than extent of surgery [6, 8, 11, 12, 15]. Khosrotehrani and Van der Ploeg presented a nomogram for prediction of prognosis in stage III B/C melanoma patients, using pathology results and age[24]. Application of this nomogram could further aid in selecting patients for SGD alone. Another preoperative aid besides the presented model could be use of the biomarker S-100B. As Kruijff et al. have shown, high serum levels of S-100B are associated with a significantly lower DFS and a trend towards worse melanoma specific survival (MSS), indicating its potential as a biomarker for clinically occult stage IV disease [25, 26]. Patients with low risk of deep pelvic nodal involvement and low S-100B could then undergo SGD alone, with regular control visits to detect early signs of deep pelvic nodal involvement (suspicious nodes on imaging/elevated S-100B). Bearing this in mind, the 16% FN rate of the presented prediction model may be allowable.

Limitations

This study is retrospective and is spread over a long timeframe. This entails inevitable alterations and improvement of imaging techniques and clinical practice over time, affecting our results. The prediction model designed for the current study has not been validated internally, due to a small sample of patients with positive deep pelvic nodes. It has to be pointed out that this model in its current state is not suited for clinical use, as there is still much to be gained from further development and testing. A prospective multicenter registration study is planned to be performed, enabling adequate data collection on all patients undergoing CGD for palpable groin metastases within a relatively small time frame. Cross validation of the presented prediction model will be performed, and its role in future clinical practice will be further defined. With the proposed prospective study, accuracy of imaging techniques can be determined more adequately.

Concerning the possible additional morbidity of a DGD; although to date no prospective randomized controlled trial (RCT) has been performed to address this, evidence exists that the additional morbidity of DGD in a CGD might be more limited than has been described in the past.[6, 22] The recently opened Australia and New Zealand Melanoma Trials Group 01.12 EAGLE FM Trial (clinicaltrials.gov identifier: NCT02166788) will hopefully provide an answer to this question. This multicenter RCT compares SGD and CGD for melanoma patients with groin metastases and no suspicious PET/CT scan.

As operating time is generally longer in a CGD, there is a potentially higher risk of surgical site infections. In a large retrospective series of Glarner et al. the number of surgical site infections is indeed significantly higher for CGDs, with an adjusted odds ratio of 2.6[27]. Once again, to gain more insight in the actual differences in morbidity between SGD and CGD, we will have to await results from the EAGLE FM Trial.

Concluding, high LNR, high number of positive inguinal nodes and inguinal ECE are risk factors for positive deep pelvic nodes in patients with palpable groin metastases of cutaneous melanoma. To date, accurate prediction of deep pelvic nodal status is suboptimal still, hence reliable selection of patients who can be spared a DGD remains difficult. Combined use of preoperative imaging and a preliminary prediction model based on histopathology results of the inguinal (superficial) part of CGD could accurately predict negative deep pelvic nodes in up to 84%. Thereby potentially identifying a group of low risk patients, in whom the extent of surgery might safely be minimized. The risk factors and the prediction model will be further investigated in a prospective multicenter registry trial for CGDs.

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Part IV – General Discussion and Summary