International Journal of Dermatology

Report

Using the Merlin assay for reducing sentinel lymph node biopsy complications in melanoma: a retrospective cohort study

Tina J. Hieken[1], MD, Mariana B. Sadurní[2], BA, Enrica Quattrocchi[2], MD, Ajdin Kobic[2], MD, Sindhuja Sominidi-Damodaran[2], MD, Jvalini T. Dwarkasing[3], PhD, Lisette Meerstein-Kessel[3], PhD, Alina G. Bridges[4], DO and Alexander Meves[2], MD

[1]Department of Surgery, Mayo Clinic, Rochester, MN, USA, [2]Department of Dermatology, Mayo Clinic, Rochester, MN, USA, [3]SkylineDx BV, Rotterdam, The Netherlands, [4]Richfield Laboratory of Dermatopathology, Dermpath Diagnostics, Cincinnati, OH, USA

Correspondence
Alexander Meves, MD
Department of Dermatology
200 First Street SW
Rochester, MN 55905
USA
E-mail: meves.alexander@mayo.edu

IRB approval status: Reviewed and approved by the Mayo Clinic IRB; approval #11-006390.

Conflict of interest: Dr. Hieken received research funding from Genentech and SkylineDx (both to Mayo Clinic). Dr. Meves received research funding from SkylineDx and has a financial interest in the Merlin assay. Dr. Dwarkasing and Dr. Meerstein-Kessel are employees of SkylineDx BV and hold stock options. All remaining authors have no conflicts of interest to declare.

Funding source: National Cancer Institute (grant K08 CA215105 to A.M.); Melanoma Research Alliance (award 652760 to EQ).

doi: 10.1111/ijd.16056

Abstract

Background The assessment of the sentinel lymph node is a cornerstone of melanoma staging. However, ~80% of sentinel lymph node biopsies (SLNB) are negative and nontherapeutic, and patients are unnecessarily exposed to surgery-related complications. Here, we gauged the potential of the Merlin assay to reduce SLNB-associated complications. The Merlin assay uses clinicopathologic variables and tumor gene expression profiling to identify low-risk patients who may forgo SLNB.

Methods We utilized the Merlin test development cohort to determine SLNB complication rates for procedures performed between 2004 and 2018 at Mayo Clinic. Complications evaluated were lymphedema, seroma, infection/cellulitis, hematoma, and wound dehiscence. Patients who underwent a completion lymph node dissection were excluded.

Results A total of 558 patients were included. The overall 90-day complication rate specific to SLNB (1 year for lymphedema) was 17.4%. The most common complications were seroma (9.3%), infection/cellulitis (4.8%), and lymphedema (4.3%). All three were more common in patients with a lower extremity primary tumor location versus other locations. With Merlin test results applied, SLNB-related complications would have decreased by 59%.

Conclusion SLNB is a safe procedure but carries a significant complication rate. Merlin testing might reduce the need for SLNB and its associated complications.

Introduction

The incidence rate of cutaneous melanoma in the United States is rising, with more than 100,350 invasive new cases and 6,850 deaths expected in 2020.[1] Currently, sentinel lymph node biopsy (SLNB) is the standard of care for clinically node-negative, intermediate thickness cutaneous melanomas. It is considered for selected patients with thinner melanomas.[2–4] SLNB status has been the most informative prognostic factor for these patients and is used to guide subsequent treatment. However, ~80% of all patients undergoing SLNB have no evident nodal metastasis.[2] These patients are exposed to the potential complications of SLNB for no apparent therapeutic benefit.[2] Therefore, new methods to identify melanoma at low

International Journal of Dermatology 2022, **61**, 848–854

risk of harboring clinically occult nodal metastases are desirable to avoid unnecessary surgery while providing the prognostic information of SLNB.[5]

We have previously reported on the Merlin assay for melanoma risk stratification.[6] This assay uses the CP-GEP model, combining clinicopathological variables with tumor gene expression profiling to identify patients who can forgo SLNB due to their low risk of nodal metastasis. The Merlin assay has been clinically validated in the United States[7] and Europe[8,9] and is commercially available for patient care. Here, we used the Merlin development cohort to determine SLNB complication rates, that is, rates of hematoma, seroma, infection/cellulitis, lymphedema, and wound dehiscence specific to the SLNB procedure. In addition, we report on the number of potentially avoidable SLNB-associated complications by applying Merlin test results to this patient cohort.

Methods

Patient cohort

The cohort consisted of 558 melanoma patients, a subset of a previous cohort used for Merlin test development.[6,7,10–12] All patients had SLNB performed within 90 days of their diagnosis. We searched the electronic medical record to retrospectively identify 855 patients with primary cutaneous melanoma who presented at Mayo Clinic tertiary care centers in Minnesota, Arizona, or Florida between 2004 and 2018 with known SLNB status.[10] We excluded patients who were SLNB-positive ($N = 203$) because SLNB-positive patients routinely underwent immediate completion lymph node dissection (CLND) before the publication of MSLT-II in 2017,[13] an extensive procedure with a high complication rate. Of note, SLNB status has been shown previously not to affect SLNB complication rates.[14] We next excluded patients who did not have their SLNB performed at Mayo Clinic's tertiary care campuses in Minnesota, Arizona, or Florida, because we did not have complete access to electronic medical records ($N = 91$). Finally, we excluded three patients with negative SLNB who underwent CLND.

Eligibility was determined based on histopathology data derived from patient medical records and established by two or more board-certified Mayo Clinic dermatopathologists.[10] We determined inclusion by the AJCC 7th edition based institutional practice guidelines of the Mayo Clinic for recommending SLNB, which were based on Breslow thickness, ulceration, mitoses, and age. Patients were eligible for this study if they met one of the following three conditions: Breslow thickness of ≥1.0 mm; Breslow thickness of 0.75–0.99 mm and presence of ulceration, mitoses, and/or age <40 years; or Breslow thickness of 0.50–0.74 mm and presence of at least two of the following: ulceration, mitoses, and age <40 years.

Exclusion criteria were: M1 distant metastatic disease within 90 days of primary melanoma diagnosis; and, for Minnesota, denial of access to medical records for research purposes (per Minnesota State law). Patient and tumor characteristics are shown in Table 1. The Mayo Clinic Institutional Review Board approved the human investigations performed in this study following the Department of Health and Human Services requirements, where appropriate.

Table 1 Patient and tumor characteristics

	No complications ($N = 461$)	With complications ($N = 97$)	*P* value[a]
Female sex, *n* (%)	174 (37.7%)	41 (42.3%)	0.41
Age at diagnosis, median (IQR)	64.2 (53.0–73.8)	64.2 (54.8–75.3)	1.00
Body mass index, mean (SD)	29.6 (6.3)	29.4 (6.4)	0.79
Diabetes mellitus, *n* (%)	41 (8.9%)	12 (12.4%)	0.29
Warfarin, *n* (%)	32 (6.9%)	10 (10.3%)	0.25
Aspirin, *n* (%)	51 (11.1%)	14 (14.4%)	0.35
Breslow depth, mm (SD)	1.6 (1.0)	1.5 (0.8)	0.11
pT stage, *n* (%)			0.46
T1	125 (27.1%)	31 (32.0%)	
T2	233 (50.5%)	51 (52.6%)	
T3	94 (20.4%)	14 (14.4%)	
T4	9 (2.0%)	1 (1.0%)	
Biopsy location, *n* (%)			**<0.001**
Head and neck	128 (31.9%)	16 (23.9%)	
Trunk	155 (37.9%)	24 (33.3%)	
Upper extremity	124 (30.9%)	23 (32.2%)	
Lower extremity	54 (14.6%)	34 (44.5%)	
Histologic type, *n* (%)			–
Superficial spreading	254 (55.1%)	56 (57.7%)	
Nodular	77 (16.7%)	13 (13.4%)	
Desmoplastic	20 (4.3%)	1 (1.0%)	
Lentigo maligna	22 (4.8%)	3 (3.1%)	
Other	88 (19.1%)	24 (24.7%)	
Number of resected basins, *n* (%)			0.18
1	400 (86.8%)	89 (91.8%)	
>1	61 (13.2%)	8 (8.2%)	
Number of SLNB removed, *n* (%)			0.08
1–2	272 (59.0%)	48 (49.5%)	
>2	189 (41%)	49 (50.5%)	

[a]Comparisons between groups were evaluated using the two-sample *t* test for continuous variables and the chi-square test or Fisher's exact test for categorical variables.

Ethnicity and race

Eighty-eight percent of study participants were non-Hispanic White, 1% were Hispanic or Latino White, 9% were of unknown reported ethnicity and White, and 2% were of unknown reported ethnicity and race.

Outcomes

Complications evaluated in this study were lymphedema, seroma, infection/cellulitis, hematoma, and wound dehiscence. Lymphedema was defined by limb girth as proposed by the American Physical Therapy Association. A noticeable difference in girth between the affected and unaffected limb within 1 year of SLNB and absent other causative factors was considered pathognomonic for lymphedema. We defined a seroma as a palpable symptomatic collection of serous fluid in the area of the lymph node surgery that occurred within 90 days of SLNB. We defined infection/cellulitis as inflammation in the area of lymph node surgery within 90 days of SLNB, which prompted antibiotic or surgical treatment. We defined a hematoma as an abnormal symptomatic collection of blood or serosanguineous fluid in the area of lymph node surgery within 90 days of SLNB. We defined dehiscence as a wound separation in the area of lymph node surgery within 90 days of SLNB. Emergency Department (ED) visits and hospital readmissions were defined as unplanned events within 30 days of SLNB.

Comorbidities

We abstracted body mass index from the SLNB procedure and sedation assessment. We defined patients on antidiabetic medications at the time of SLNB, including insulin, metformin, glimepiride, glyburide, glipizide, or sitagliptin, as having diabetes mellitus. We identified patients who were treated with warfarin before SLNB by chart review. Per institutional guidelines, patients were asked to discontinue warfarin 3 days before surgery. We identified patients on aspirin (any daily dose) by review of the electronic medical record.

Merlin assay

The Merlin assay is now commercially available from SkylineDx (San Diego, CA, USA). Merlin assay results were obtained as previously described using the CP-GEP model[6] and used here to calculate hypothetical reductions in SLNB and SLNB-related complications for 547 of the 558 patients studied. Eleven patients did not have Merlin assay results available. The CP-GEP model combines the expression of eight genes in the primary tumor with patient age and Breslow depth to assess the risk of SLN metastasis.

Table 2 SLNB complications

SLNB complications	
Based on all patients (N = 558)	
Any complication, *n* (%)	97 (17.4)
Seroma, *n* (%)	52 (9.3)
Lymphedema, *n* (%)	24 (4.3)
Infection/cellulitis, *n* (%)	27 (4.8)
Hematoma, *n* (%)	18 (3.3)
Dehiscence, *n* (%)	14 (2.5)
Emergency room visits, post-procedure, *n* (%)	6 (1.1)
Readmitted to the hospital, post-procedure, *n* (%)	9 (1.6)
Based on subset of patients with lymphedema (N = 24)	
Days from SLNB to diagnosis, median (range)	46 (2, 314)
Referred to PT, *n* (%)	14 (58.3)
Multiple follow-up visits in PT, *n* (%)	6 (25.0)
Ultrasound to rule out DVT, *n* (%)	6 (25.0)
Based on subset of patients with a seroma (N = 52)	
Days from SLNB to diagnosis, median (range)	10 (1, 50)
Seromas aspirated or drained, *n* (%)	36 (69.2)
Seroma, ml aspirated, median (range)	50 (2, 255)
Seroma catheter placed (e.g., Penrose drain), *n* (%)	8 (15.4)
Placed on antibiotic therapy, *n* (%)	13 (25.0)
Based on subset of patients with infection/cellulitis (N = 27)	
Days from SLNB to diagnosis, median (range)	17 (1, 79)
Placed on antibiotic therapy, *n* (%)	27 (100)
Based on subset of patents with a hematoma (N = 18)	
Days from SLNB to diagnosis, median (range)	9 (0, 32)
Placed on antibiotic therapy, *n* (%)	6 (33.3)

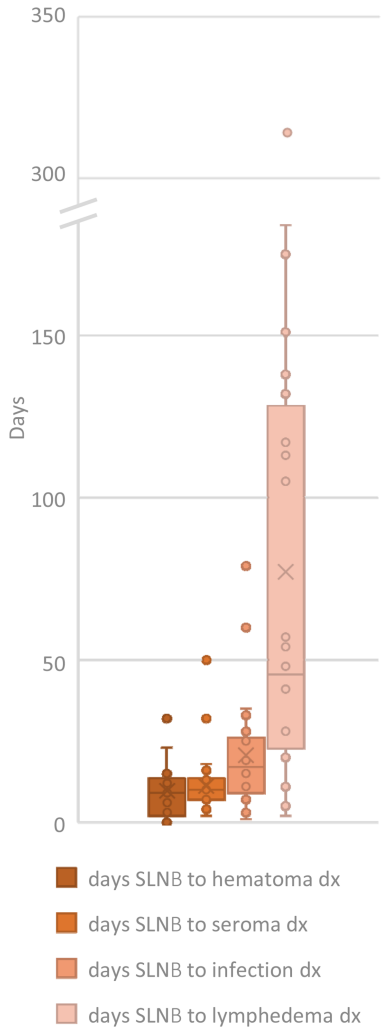

Figure 1 Time to complications after sentinel lymph node biopsy (SLNB). Data are visualized as box plots

Table 3 Clinical variables associated with SLNB complications

	Hematoma			Seroma			Infection/cellulitis			Lymphedema		
	Yes (*N* = 18)	**No (*N* = 540)**	***P* value[a]**	**Yes (*N* = 52)**	**No (*N* = 506)**	***P* value[a]**	**Yes (N = 27)**	**No (N = 531)**	***P* value[a]**	**Yes (N = 24)**	**No (N = 534)**	***P* value[a]**
Female gender, *n* (%)	4 (22.2)	211 (39.1)	0.22	22 (42.3)	193 (38.1)	0.56	14 (51.9)	201 (37.9)	0.15	16 (66.7)	199 (37.3)	**0.004**
Age at diagnosis, mean (SD)	64.7 (16.6)	61.5 (15.9)	0.41	60.4 (15.8)	61.8 (16.0)	0.54	60.2 (17.2)	61.7 (15.9)	0.63	61.6 (18.3)	61.6 (15.8)	0.99
Body mass index, mean (SD)	29.6 (6.2)	29.6 (6.3)	0.99	28.7 (6.5)	29.6 (6.3)	0.47	29.7 (6.7)	29.6 (6.3)	0.95	29.3 (6.6)	29.5 (6.1)	0.82
Primary melanoma location, *n* (%)			0.07			**<0.001**			**<0.001**			**<0.001**
Head/neck	9 (50.0)	134 (24.8)		5 (9.6)	138 (27.3)		1 (3.7)	142 (26.7)		1 (4.2)	142 (26.6)	
Trunk	2 (11.1)	177 (32.8)		14 (26.9)	165 (32.6)		8 (29.6)	171 (32.2)		3 (12.5)	176 (33.0)	
Upper extremities	4 (22.2)	144 (26.7)		15 (28.9)	133 (26.3)		4 (14.8)	144 (27.1)		3 (12.5)	145 (27.2)	
Lower extremities	3 (16.7)	85 (15.7)		18 (34.6)	70 (13.8)		14 (51.9)	74 (13.9)		17 (70.8)	71 (13.3)	
Number of resected basins, *n* (%)			0.26			0.18			**0.04**			0.34
1	14 (88.0)	475 (77.8)		49 (87.0)	440 (94.2)		27 (100)	462 (87.0)		23 (95.8)	466 (87.3)	
>1	4 (12.0)	65 (22.2)		3 (13.0)	66 (5.8)		0	69 (13.0)		1 (4.2)	68 (12.7)	
No. of SLNB removed, *n* (%)			0.11			0.41			0.55			0.46
1–2	7 (38.9)	313 (58.0)		27 (51.9)	293 (57.9)		14 (51.9)	306 (57.6)		12 (50.0)	308 (57.7)	
>2	11 (61.1)	227 (42.0)		25 (48.1)	213 (42.1)		13 (48.1)	225 (42.4)		12 (50.0)	226 (42.3)	
Hematomas, *n* (%)	–	–	–	3 (5.8)	15 (3.0)	0.23	0	18 (3.4)	1.00	1 (4.2)	23 (3.8)	0.61
Seromas, *n* (%)	3 (16.7)	49 (9.0)	0.23	–	–	–	14 (51.9)	38 (7.2)	**<0.001**	10 (41.7)	42 (7.9)	**<0.001**
Infection/cellulitis, *n* (%)	0	27 (5.0)	1.00	14 (26.9)	13 (2.6)	**<0.001**	–	–	–	5 (20.8)	22 (4.1)	**<0.001**
Lymphedema, *n* (%)	1 (5.6)	23 (4.3)	0.61	10 (19.2)	14 (2.77)	**<0.001**	5 (18.5)	19 (3.6)	**<0.001**	–	–	–
Diabetes, *n* (%)	4 (22.2)	49 (9.1)	0.08	3 (5.8)	50 (9.9)	0.46	2 (7.4)	51 (9.6)	1.00	4 (16.7)	49 (9.2)	0.27
Warfarin, *n* (%)	4 (22.2)	38 (7.0)	**0.04**	4 (7.7)	38 (7.5)	1.00	2 (7.4)	40 (7.5)	1.00	2 (8.3)	40 (7.5)	0.70
Aspirin, *n* (%)	4 (22.2)	61 (11.3)	0.15	8 (15.4)	58 (11.3)	0.38	3 (11.1)	62 (13.2)	1.00	4 (16/7)	61 (11.4)	0.51

[a]Comparisons between groups were evaluated using the two-sample *t* test for continuous variables and the chi-square test or Fisher's exact test for categorical variables.

Statistical analysis

We performed statistical analysis with XLSTAT version 2020.1.3 (Addinsoft Inc., New York, NY, USA). Data were summarized using standard descriptive statistics. We evaluated comparisons between continuous variables by the two-sample *t* test. The chi-square or Fisher's exact test were used for categorical variables. All calculated *P* values were two-sided, and *P* values <0.05 were considered statistically significant.

Results

We included 558 patients who underwent SLNB within 90 days of their melanoma diagnosis between 2004 and 2018 in the analysis. Overall, 97 (17.4%) of 558 patients developed at least one complication (Table 2). Seroma was the most common complication with 52 (9.3%) patients affected within 90 days of SLNB, followed by infection/cellulitis in 27 (4.8%) patients within 90 days of SLNB, and lymphedema in 24 (4.3%) patients within 1 year of SLNB. Eighteen (3.3%) patients developed a hematoma within 90 days of SLNB. The least common complication was wound dehiscence, with 14 (2.5%) patients affected within 90 days of SLNB. Six of 558 (1.1%) patients sought help in an ED within 30 days of surgery. Three ED visits were for seromas, infection/cellulitis, or both, but none of these required intravenous antibiotics; two were for bleeding, one was for hypertension and volume overload. Of the 558 patients, nine (1.6%) were readmitted to the hospital within 30 days of SLNB. Five readmissions were for infections requiring intravenous antibiotics (piperacillin–tazobactam and vancomycin). Four readmissions returned to the operating room: one was for a groin seroma evacuation, three were for hematoma evacuations and pain control.

We next examined the time to event for SLNB complications. Hematomas developed first with a median time to diagnosis of 9 days after SLNB (range 0–32 days), followed by seromas, which were noted at a median of 10 days (range 1–50 days) postoperatively. Infection/cellulitis developed at a median of 17 days after SLNB (range 1–79 days). Lastly, lymphedema developed at a median of 46 days after SLNB (range 2–314 days) (Fig. 1). No significant differences in time to event were noted for patients 65 years and older compared to patients younger than 65 years.

Concerning therapy, most seromas, 36 (69.2%) of 52, were treated with simple aspiration. A drain was placed for eight patients (15.4%) (Table 2). Thirteen (25%) seroma patients received antibiotic therapy, including doxycycline, trimethoprim/sulfamethoxazole, cefalexin, or amoxicillin/clavulanic acid. Four patients (7.7%) required intravenous piperacillin–tazobactam and vancomycin in the hospital. All patients with lymphedema were referred to physical therapy per institutional protocols, and a physical therapy lymphedema consult was documented in 14 of 24 patients (58.3%). A quarter of

Table 4 SLNB complications with Merlin test decisions applied

	All Ages			<65 years at melanoma diagnosis			≥65 years at melanoma diagnosis		
SLNB complications	**Reference**	**With Merlin decisions applied**	**% reduction in SLNB complications**	**Reference**	**With Merlin decisions applied**	**% reduction in SLNB complications**	**Reference**	**With Merlin decisions applied**	**% reduction in SLNB complications**
Total patients, *n* (%)	558 (100)	547 (100)	–	296 (100)	291 (100)	–	262 (100)	256 (100)	–
Low-risk Merlin test results, *n* (%)	–	279 (51.0)	–	–	138 (47.4)	–	–	141 (55.1)	–
Undergoing SLNB, *n* (%)	558 (100)	268 (49.0)	51.0	296 (100)	153 (52.6)	47.4	262 (100)	115 (44.9)	55.1
Any complication, *n* (%)	97 (17.4)	39 (7.1)	59.2	52 (17.6)	20 (6.9)	61.5	45 (17.2)	19 (7.4)	57.0
Seroma, *n* (%)	52 (9.3)	16 (2.9)	68.8	32 (10.8)	10 (3.4)	68.5	20 (7.6)	6 (2.3)	69.7
Lymphedema, *n* (%)	24 (4.3)	10 (1.8)	58.1	11 (3.7)	3 (1.0)	72.7	13 (5.0)	7 (2.7)	46.2
Infection/cellulitis, *n* (%)	27 (4.8)	14 (2.6)	45.8	13 (4.4)	6 (2.1)	52.3	14 (5.3)	8 (3.1)	41.5
Hematoma, *n* (%)	18 (3.3)	6 (1.1)	66.7	7 (2.4)	2 (0.7)	70.8	11 (4.2)	4 (1.6)	61.9
Dehiscence, *n* (%)	14 (2.5)	7 (1.3)	50.0	11 (3.7)	7 (2.4)	35.1	3 (1.2)	0	100
Emergency department visits, post-procedure, *n* (%)	6 (1.1)	0	100	3 (1.0)	0	100	3 (1.2)	0	100
Readmission to the hospital, post-procedure, *n* (%)	9 (1.6)	5 (0.9)	43.8	2 (0.7)	2 (0.7)	0	7 (2.7)	3 (1.2)	55.6

lymphedema patients, six of the 24 (25%), had multiple visits with physical therapy at Mayo Clinic. Of the 24 lymphedema patients, six (25%) underwent compression ultrasonography with Doppler to rule out deep vein thrombosis and tested negative. All patients with infection/cellulitis were placed on antibiotic therapy, most commonly cefalexin, followed by doxycycline, trimethoprim/sulfamethoxazole, amoxicillin/clavulanic, and cefadroxil. Five patients (18.5%) required intravenous piperacillin–tazobactam and vancomycin in the hospital. One patient was treated with intravenous clindamycin in the ED.

We next sought to identify patient and tumor characteristics associated with SLNB complications. Interestingly, in univariate analysis, we found that seromas, infection/cellulitis, and lymphedema are associated events, whereas hematomas occurred independently (Table 3). Lymphedema developed predominantly in patients with a lower extremity melanoma and in females. Hematomas were associated with warfarin use, even though all patients had discontinued warfarin 3 days before surgery. While seromas, infection/cellulitis, and lymphedema developed most frequently in the inguinal region, most hematomas occurred in the head and neck area.

Lastly, we aimed to quantify the extent to which the Merlin assay, a recently introduced molecular test to identify patients who may safely forgo the SLNB surgery, could reduce SLNB-associated complications.[3,6] Merlin test results were obtained for 547 of the 558 patients analyzed. Of the 558 patients, 279 (51%) had a Merlin low-risk result. Omission of SLNB in these 279 patients would have decreased complications proportionately, namely by 59.2% in our cohort (Table 4). Hypothetical reductions in SLNB complication rates achieved by Merlin testing in patients aged 65 and older were comparable to reductions in patients younger than 65.

Discussion

Our data shows that SLNB-related complications are relatively common. A previous meta-analysis of SLNB complications in 9047 patients reported an overall complications rate of 11.3% (95% CI: 8.1–15).[15] However, there was little uniformity in the definition of variables across the analyzed studies, including follow-up time. The overall complication rate here was significantly higher at 17.4% but in line with the 20.4% complication rate previously reported for a large German academic hospital system.[14] The relatively low complication rate identified by meta-analysis can be attributed to inconsistencies in defining SLNB complications.[15] In our cohort, we observed no SLNB-associated death or serious morbidity, such as myocardial infarction, thromboembolism, or stroke.

Consistent with previous reports,[14,15] we found that seroma was the most common complication, followed by infection/cellulitis and lymphedema. The reported crude seroma rate in the literature ranges from 0 to 38% versus 9.3% at our institution.[15] The reported infection/cellulitis rate ranges from 0.3 to 19% in the literature[15] versus 4.8% in the current study, and lymphedema ranges from 0 to 17% across prior studies compared to the 4.3% rate observed here. Complication rates derived from our cohort are thus within the ranges previously reported.

Interestingly, we found that seroma, infection/cellulitis, and lymphedema were associated events. Moreover, lymphedema was more frequently observed in females and for primary melanomas of the lower extremities. Female patients with a lower extremity melanoma who develop an infected seroma appear to be at the highest risk for lymphedema. This observation is in line with previous reports.[14,16–19] Contrasting previous findings,[14] we did not identify male sex as an independent risk factor for seroma formation. Likewise, body mass index, patient

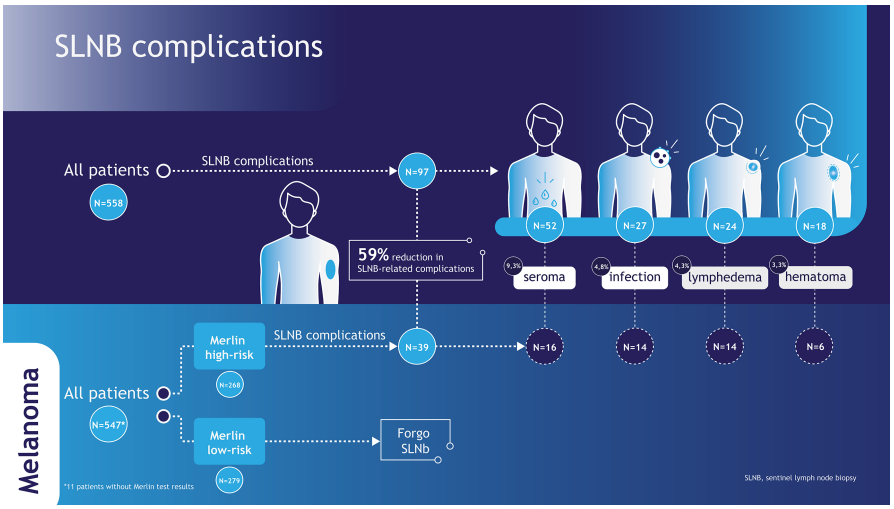

Figure 2 Graphical summary of study results

age at SLNB, and a greater number of resected lymph nodes and lymph node basins were not associated with developing complications, as was reported by some[18–22] but not by other investigators.[17,19,23,24]

In conclusion, SLNB is a safe procedure but does have a defined complication rate. Many complications are self-limited, while others require additional interventions. The Merlin assay, which has been validated retrospectively in multiple independent cohorts[7–9] and is currently undergoing prospective validation in a multicenter study (NCT04759781), reduced the need for SLNB by over 50% in this cohort and complications by 59% (Fig. 2). Using the Merlin test to omit SLNB in low-risk patients is expected to decrease postoperative morbidity without sacrificing oncologic safety.

References

1 Cancer stat facts: melanoma of the skin. National Cancer Institute: Surveillance, Epidemiology, and End Results Program. https://seer.cancer.gov/statfacts/html/melan.html (accessed 21 December 2020).
2 Morton DL, Thompson JF, Cochran AJ, *et al*. Final trial report of sentinel-node biopsy versus nodal observation in melanoma. *N Engl J Med* 2014; **370**: 599–609.
3 National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Melanoma: Cutaneou. http://paperpile.com/b/MxWm0E/Pup0c1.2021. 25 November 2020.
4 Gershenwald JE, Scolyer RA, Hess KR, *et al*. Melanoma staging: evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual. *CA Cancer J Clin* 2017; **67**: 472–492.
5 Meves A, Eggermont AMM. Deselecting melanoma patients for sentinel lymph node biopsy during COVID-19: clinical utility of tumor molecular profiling. *Mayo Clin Proc Innov Qual Outcomes* 2020; **4**: 586–587.
6 Bellomo D, Arias-Mejias SM, Ramana C, *et al*. Model combining tumor molecular and clinicopathologic risk factors predicts sentinel lymph node metastasis in primary cutaneous melanoma. *JCO Precis Oncol* 2020; **4**:319–334.
7 Yousaf A, Tjien-Fooh FJ, Rentroia-Pacheco B, *et al*. Validation of CP-GEP (Merlin Assay) for predicting sentinel lymph node metastasis in primary cutaneous melanoma patients: a U.S. cohort study. *Int J Dermatol* 2021; **60**: 851–856.
8 EEAP M, Dwarkasing JT, Tempel D, *et al*. Validation of a clinicopathological and gene expression profile model for sentinel lymph node metastasis in primary cutaneous melanoma. *Br J Dermatol* 2021;**184**:944–951. https://doi.org/10.1111/bjd.19499
9 Johansson I, Tempel D, Dwarkasing JT, et al. Independent validation study of a CP-GEP model (Merlin Assay) to identify patients with melanoma who can safely forgo sentinel lymph node biopsy. *Eur J Surg Oncol* S0748-7983(21)00814-3. https://doi.org/10.1016/j.ejso.2021.11.010
10 Eggermont AMM, Bellomo D, Arias-Mejias SM, *et al*. Identification of stage I/IIA melanoma patients at high risk for disease relapse using a clinicopathologic and gene expression model. *Eur J Cancer* 2020; **140**: 11–18.
11 Bellomo D, Bridges AG, Hieken TJ, *et al*. Reply to E K Bartlett et al and A H R Varey et al. *JCO Precis Oncol* 2020; **4**:992–994.
12 Quattrocchi E, Sominidi-Damodaran S, Murphree DH, *et al*. β3 integrin immunohistochemistry as a method to predict sentinel lymph node status in patients with primary cutaneous melanoma. *Int J Dermatol* 2020; **59**: 1241–1248.
13 Faries MB, Thompson JF, Cochran AJ, *et al*. Completion dissection or observation for sentinel-node metastasis in melanoma. *N Engl J Med* 2017; **376**: 2211–2222.
14 Persa O-D, Knuever J, Rose A, *et al*. Predicting risk for seroma development after axillary or inguinal sentinel lymph node biopsy in melanoma patients. *Int J Dermatol* 2019; **58**: 185–189.
15 Moody JA, Ali RF, Carbone AC, *et al*. Complications of sentinel lymph node biopsy for melanoma - a systematic review of the literature. *Eur J Surg Oncol* 2017; **43**: 270–277.
16 Wrightson WR, Wong SL, Edwards MJ, *et al*. Complications associated with sentinel lymph node biopsy for melanoma. *Ann Surg Oncol* 2003; **10**: 676–680.
17 Ellis MC, Weerasinghe R, Corless CL, *et al*. Sentinel lymph node staging of cutaneous melanoma: predictors and outcomes. *Am J Surg* 2010; **199**: 663–668.
18 Wasserberg N, Tulchinsky H, Schachter J, *et al*. Sentinel-lymph-node biopsy (SLNB) for melanoma is not complication-free. *Eur J Surg Oncol* 2004; **30**: 851–856.
19 Ling A, Dawkins R, Bailey M, *et al*. Short-term morbidity associated with sentinel lymph node biopsy in cutaneous malignant melanoma. *Australas J Dermatol* 2010; **51**: 13–17.
20 Stuiver MM, Westerduin E, ter Meulen S, *et al*. Surgical wound complications after groin dissection in melanoma patients – a historical cohort study and risk factor analysis. *Eur J Surg Oncol* 2014; **40**: 1284–1290.
21 Roaten JB, Pearlman N, Gonzalez R, *et al*. Identifying risk factors for complications following sentinel lymph node biopsy for melanoma. *Arch Surg* 2005; **140**: 85–89.
22 Wilke LG, McCall LM, Posther KE, *et al*. Surgical complications associated with sentinel lymph node biopsy: results from a prospective international cooperative group trial. *Ann Surg Oncol* 2006; **13**: 491–500.
23 Lucci A, McCall LM, Beitsch PD, *et al*. Surgical complications associated with sentinel lymph node dissection (SLND) plus axillary lymph node dissection compared with SLND alone in the American College of Surgeons Oncology Group Trial Z0011. *J Clin Oncol* 2007; **25**: 3657–3663.
24 Cigna E, Gradilone A, Ribuffo D, *et al*. Morbidity of selective lymph node biopsy for melanoma: meta-analysis of complications. *Tumori* 2012; **98**: 94–98.

