Immediate post-Mohs micrographic surgery adverse events: A Spanish multicentre prospective cohort study (Regesmohs)

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Introduction

Mohs micrographic surgery (MMS) is a technique that provides high cure rates and great degree of tissue sparing. It is widely introduced in US and Australia and has been introduced in Spain more recently. MMS is reported to be very safe, with low incidence of postoperative adverse events.[1,2] Two large american studies have recently confirmed that MMS is associated with a low risk for minor complications and a rare risk for serious adverse events. Due to the low incidence of adverse effects, large numbers of cases have to be included to obtain reliable data for specific complications and to make statistical comparisons.

Objective

To describe the prevalence of immediate post-surgical adverse events and their association with several candidate risk factors in patients undergoing MMS in a Spanish cohort.

Methods

The Regesmohs is a prospective observation registry including consecutive patients ungergoing MMS in 17 Spanish centres started in July 2013. The information is collected through an online data collection system (OpenClinica, version 3.1) of the Research Unit of the Spanish Academy of Dermatology. All investigators use a common dictionary data to ensure uniformity in the definition of the variables. The registry has a continuous online monitoring system that detects missing or inconsistent data. Regesmohs received ethical approval from *Comité Etico de Investigación Clínica de Navarra* (E011/2013) and all patients gave their informed consent to participate. Participating centres include all consecutive patients tributary of MMS. Several candidate risk factors for post-surgery morbidity were registered: genre, age, anatomical area, immunosupression, diabetes mellitus, type of anesthetic, depth of the tumor, type of closure, defect size, repair technique, antiplatelets and/or anticoagulant intake and intrasurgical morbility (hemorrhage that required surgery discontinuation, hypertension, arrythmia, vasovagal syncope). The following immediate post-surgery events are registered in patients from the study: bleeding that requires medical intervention, wound infection (defined by "infection that requires treatment"), flap/graft necrosis and, wound dehiscence. Comparisons between the variables were performed using the Chi-square test or Fisher´s exact test when appropriate. A two sample t test was used to evaluate numerical variables. Statistical analysis was performed using Stata (StataCorp. 2015 Release 14.2).

Results

A cohort of 1986 patients with 1986 lesions excised with MMS was recorded. The mean time to register post-surgery morbidity was 0.88 months. Patient and tumor characteristics are summarised in table 1. We observed adverse events in 148 patients (7.6%) with no serious events registered. The prevalence of registered immediate postsurgical adverse efects were as follows: bleeding 0.95% (19 cases), wound infection 1.25% (25 cases), flap/graft necrosis 2.5 % (51 cases) and wound dehiscence 1.3% (26 cases). Forty three cases (2.16%) showed other complications (mainly alterations in wound healing such as trap door). Postsurgical adverse events were significantly associated to tumour depth, defect repair technique, use of antiplatelets and/oranticoagulants, area of the defect, presence of surgical adverse events during the surgery, and use of general anesthesia in the univariate analysis (table 2). On the multivariate analysis, several variables were included (table 3), but only the following were independent variables associated to an increased incidence of adverse posturgical events: defect repair technique (flaps or complex closures), use of antiplatelets and/or anticoagulants, area of the defect and presence of surgical adverse events during the surgery (table 3).

Table 1

Patient/lesion characteristics	Mean (SD) or no. of cases (percentage)
Mean age (years)	68 (14)
Gender	
Male	1013 (51)
Immunosuppression	
Yes	70 (3.5)
Diabetes	
Yes	211 (10)
Anticoagulant and/or antiplatelet	
Yes	331 (16.8)
Mean defect size (cm^2)	6.2 (11.9)
Tumor type	
Basal cell carcinoma	1726 (86.9)
Squamous cell carcinoma	126 (6.3)
Other	134 (6.7)
Primary / recurrence	
Primary	1282 (64.5)
Recurrence	410 (20.4)
Persistence	294 (14.8)
General anesthetics	
Yes	173 (8.7)
Surgery (conventional/paraffine)	
Conventional	1789 (90)
Paraffine	187 (9.4)
Number of stages	
1	1057 (57.8)
2	565 (30.8)
3	207 (11.3)

Table 2

	Posturgical adverse events No (%)	Yes (%)	p
Tumour depth			
Epidermis	48/1788 (3)	2/145 (1)	
Dermis	944/1788 (53)	80/145 (55)	
Hypodermis	628/1788 (35)	33/145 (23)	
Fascia	41/1788 (2)	3/145 (2)	
Muscular	118/1788 (7)	23/145 (16)	
Bone	9/1788 (1)	4/145 (3)	**<0.01**
General anesthesia			
Yes	151/1838 (8)	22/148 (15)	**<0.01**
Repair technique			
Second intention	216/1838 (12)	7/148 (5)	
Primary closure	540/1838 (29)	28/148 (19)	
Flap	798/1838 (43)	78/148 (53)	
Graft	234/1838 (13)	19/148 (13)	
Complex closure	50/1838 (3)	16/148 (11)	**<0.01**
Antiaplatelets/anticoagulants			
Yes	291/1815 (16)	40/146 (27)	**<0.01**
Genre			
Male	930/1838 (51)	83/148 (56)	0.1993
Immunosupression			
Yes	61/1838 (3)	9/148 (6)	0.0796
Corticosteroids			
Yes			
Diabetes Mellitus			
Yes	194/1800 (11)	17/147 (12)	0.7679
Subtype of tumour			
Basal cell carcinoma	1598/1838 (87)	128/148 (86)	
Squamous cell carcinoma	114/1838 (6)	12/148 (8)	
Other	126/1838 (7)	8/148 (5)	0.5450
Primary/recurrence/persistence			
Primary	1182/1838 (64)	100/148 (68)	
Recurrence	389/1838 (21)	21/148 (14)	
Persistence	267/1838 (15)	27/148 (18)	0.0939
Localization (risk)			
Low	1416/1835 (77)	116/148 (78)	
Medium	382/1835 (21)	27/148 (18)	
Low	37/1835 (2)	5/148 (3)	0.4348

Table 3

	Relative Risk for Posturgical adverse events Univariate		Multivariate	
Tumour depth	**RR (CI 95%)**	**p**	**RR (CI 95%)**	**p**
Epidermis	Reference			
Dermis	1.95 (0.49-7.72)	0,340		
Hypodermis	1.25 (0.31-5.05)	0,756		
Fascia	1.7 (0.3-9.74)	0,549		
Muscular	4.08 (1-16.67)	0,050		
Bone	7.69 (1.58-37.49)	0,012		
General anesthesia				
No	Reference			
Yes	1.83 (1.2-2.8)	0,005		
Repair technique				
Second intention	Reference		Reference	
Primary closure	1.57 (0.7-3.54)	0,277	1.38 (0.61-3.14)	0,441
Flap	2.84 (1.33-6.06)	0,007	2.58 (1.21-5.49)	0,014
Graft	2.39 (1.02-5.58)	0,044	1.67 (0.71-3.9)	0,240
Complex closure	7.72 (3.32-17.97)	0,000	5.79 (2.54-13.16)	0,000
Antiplatelets/anticoagulants				
No	Reference		Reference	
Yes	1.86 (1.32-2.62)	0,000	1.75 (1.23-2.48)	0,002
Age	1 (0.99-1.01)	0,937	0.99 (0.98-1)	0,273
Area	1.01 (1.01-1.02)	0,000	1.01 (1.01-1.02)	0,000
Surgical adverse events				
No	Reference		Reference	
Yes	3.03 (1.55-5.95)	0,001	1.99 (1-3.96)	0,050

Limitations

The low incidence rates of postsurgical complications precluded the statistical evaluation between each specific adverse event (bleeding, wound infection, necrosis and dehiscence) and their hypothetical causes (antiplatelets, immunosupression, tumour depth, etc). Moreover, antiplatelets and anticoagulants were evaluated as a whole group. Finally, the mean time to event register was long (close to one month) and may have induced an underestimation of adverse effects.

Discussion

We detected a total adverse event rate of almost 8%. When categorised by subtype of adverse events, our results are similar to those previously reported in the literature.[1-8] The most frequent postsurgical complication in our series was flap or graft partial necrosis. Similarly, bleeding and wound infection were usually mild and were managed medically with no sequelae. This is the first large prospective Spanish study of adverse events in MMS. We conclude that MMS can be considered a safe technique.

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