Validating the effectiveness of the International Myositis Assessment and Clinical Studies Group (IMACS) idiopathic inflammatory myopathy cancer screening guidelines in a Singapore cohort

Sir,

Idiopathic inflammatory myopathies (IIM) confer patients a 5-to-14-fold risk of malignancy compared to general population (1, 2). Anti-TIF1g antibody-positive patients have the highest risk, with 19.1-fold higher odds compared to antibody-negative patients (3). The International Myositis Assessment and Clinical Studies Group (IMACS) recommended a set of cancer screening guidelines for IIM patients in November 2023 (4). We validated the guidelines in a Singapore cohort.

We retrospectively reviewed consecutive adult IIM patients seen at a tertiary hospital in Singapore from 1 January 2015 to 30 June 2021. All subjects fulfilled Bohan/Peter criteria for definite or probable IIM, and were sub-classified into IIM-subtypes based on 2017 ACR/EULAR classification criteria for IIM, 2017 ENMC criteria for immune-mediated necrotising myopathy (IMNM), Connors/Solomon's criteria for anti-synthetase syndrome (ASyS) and overlap myositis (OM) for those with underlying connective tissue disease or myositis-associated antibody otherwise not defined in other diagnostic categories. Subjects were cancer risk-stratified according to IMACS guidelines. Cancer-associated myositis (CAM) was defined as cancer diagnosis occurring within 3 years before or after IIM-diagnosis.

Of 119 IIM subjects, 57% had dermatomyositis (DM), 24% ASyS, 15% OM, 4% IMNM. 33% were males, 79% Chinese and median age was 58.0 (IQR 45.5-63.0) at IIM-diagnosis. Anti-TIF1γ (33%) was the most common myositis specific antibody (MSA).

Applying IMACS guidelines, 77/119 were classified as high-risk (HR), 32/119 moderate-risk (MR) and 10/119 standard risk for cancer. In the HR group, 86.3% had DM, 32.9% male, median age 59.0 (IQR 49.0-65.0), 39.7% had dysphagia, and anti-TIF1γ (53.4%) was the most common MSA followed by anti-MDA5 (27.4%). The HR group had a median of 3 high-risk factors.

In the MR group, most had ASyS (47.2%), 41.7% were male and median age was 55.0 (IQR 45.5-60.3).

All 31/199 subjects with cancer in their lifetime were stratified into HR and MR groups. 25 subjects had CAM, and 23 were HR. 2 CAM subjects developed cancer beyond 6 months after IIM-diagnosis (Table I).

In our cohort, IMACS guidelines effectively stratified CAM into HR/MR groups, in whom enhanced cancer screening would be offered to detect concurrent malignancy. However, the positive predictive values (PPVs) for CAM were low at 0.30 and 0.06 for HR and MR groups respectively and was lower at 0.22 for the HR group if patients with cancer diagnosed before IIM-diagnosis were excluded. Our findings were similar to those reported by Stone *et al*. (5) and Teh *et al*. (6) in two predominantly Caucasian populations where CAM were stratified into HR and MR groups but PPVs were low (HR: 0.08-0.15; MR: 0.02-0.1).

Both CAM patients who developed cancer after initial enhanced cancer screening were both in the HR group and had anti-TIF1g positive DM with dysphagia. 1 had breast cancer at 20 months, the other developed nasopharyngeal carcinoma at 22 months post-IIM diagnosis. They were diagnosed during continual enhanced cancer screening that included annual mammogram and 4-6 monthly otorhinolaryngology reviews

Table I. Characteristics of local IIM cohort after cancer risk-stratification.

		High risk for CAM[√] (n=73)	Moderate risk for CAM[√] (n=36)	Standard risk for CAM (n=10)	*p*-value
Demographics					
Gender	Male[μ], n (%)	24 (32.9)	15 (41.7)	0 (0)	0.036
Ethnicity	Chinese, n (%)	57 (78.1)	28 (77.8)	9 (90)	0.413
	Malay, n (%)	11 (15.1)	7 (19.4)	0 (0)	
	Indian, n (%)	4 5.5)	0 (0)	1 (10)	
	Others, n (%)	1 (1.4)	1 (2.8)	0 (0)	
Age at diagnosis, median years (IQR)		59 (49.0 – 65.0)	56.5 (46.0 – 61.5)	35.0 (28.0 – 38.0)	<0.001
IIM characteristics					
IIM-subtype					
Dermatomyositis[ς], n (%)		63 (86.3)	5 (13.9)	0 (0)	<0.001
Anti-synthetase syndrome[∞], n (%)		6 (8.2)	17 (47.2)	5 (50)	
Overlap myositis[∞], n (%)		3 (4.1)	11 (30.6)	4 (40)	
Immune-mediated necrotising myopathy[μ], n (%)		1 (1.4)	3 (8.3)	1 (10)	
MSA/MAA present					
Anti-TIF1[ς], n (%)		39 (53.4)	0 (0)	0 (0)	<0.001
Anti-NXP2[ς], n (%)		4 (5.5)	0 (0)	0 (0)	0.510
Anti-SAE1[μ], n (%)		2 (2.7)	0 (0)	0 (0)	1.000
Anti-Mi 2[μ], n (%)		7 (9.6)	3 (8.3)	0 (0)	0.886
Anti-MDA5[μ], n (%)		20 (27.4)	4 (11.1)	0 (0)	0.032
Anti-SRP[∞], n (%)		3 (4.1)	4 (11.1)	1 (10)	0.272
Anti-Jo1[∞], n (%)		4 (5.5)	11 (30.6)	2 (20)	0.001
Non-Jo1 ASyS antibodies, n (%)		10 (13.7)	12 (33.3)	3 (30)	0.04
Clinical features					
Dysphagia[ς], n (%)		29 (39.7)	0 (0)	0 (0)	<0.001
Diagnosis of cancer anytime, n (%)		28 (38.4)	3 (8.6)	0 (0)	<0.001
CAM, n (%) 23 (31.5)		2 (5.6)	0 (0)	0 001	
Details of IIM-related cancer					
Time from cancer diagnosis to IIM diagnosis					
≤ 3 years before, n (%)		6 (26.1)	0 (0)	0 (0)	
≤ 6 months after IIM, n (%)		15 (65.2)	2 (100)	0 (0)	
6-36 months after IIM, n (%)		2 (8.7)	0 (0)	0 (0)	
Type of cancers					
Breast, n (%) 8 (34.8)		0 (0)	0 (0)		
Nasopharyngeal carcinoma, n (%)		6 (26.1)	1 (50.0)	0	
Bowel, n (%) 2 (8.7)		0 (0)	0		
Gynaecological (non-ovarian), n (%)		2 (8.7)	0 (0)	0	
Prostate, n (%)		0 (0)	1 (50.0)	0	
Other, n (%)		5[ε] (21.8)	0 (0)	0	

[√] Subjects with ≥2 'High risk' factors are considered high risk for IIM-related cancer, while subjects with ≥2 'Intermediate risk' factors or 1 'High risk' factor are considered moderate risk for IIM-related cancer. In the HR group, proportion of cancer occurrences increased with number of high-risk factors (HRFs) present: 1/1 with 5 HRFs, 10/13 with 4 HRFs, 14/29 with 3 HRFs, and 3/34 with 2 HRFs. Both MR group CAM patients had 1 HRF.

[ε] 1 Tonsillar Ca, 1 Renal Ca, 2 Lung Ca, 1 Thyroid Ca.

[ς] IMACS High risk factor for malignancy.

[μ] IMACS Intermediate risk factor for malignancy.

[∞] IMACS Low risk factor for malignancy.

• 3 subjects in the high-risk group developed malignancies more than 3 years before onset of IIM. 2 subjects in the high-risk group developed malignancy more than 3 years after diagnosis of IIM.

offered to anti-TIF1g-positive DM patients at our centre for up to 3 years post-IIM diagnosis. Both cases exemplified the need for continued vigilance for cancer in the first 3 years post-IIM diagnosis, especially in the HR group where yearly basic panel suggested by IMACS guidelines may be insufficient.

We show that IMACS cancer screening guidelines effectively stratified cancer risk in our cohort, however the PPV for CAM was low, which suggests that applying enhanced screening universally may lead to unnecessary investigations and increased healthcare costs. More selective, risk-tailored assessments such as regular mammography and naso-endoscopy may be required for specific high-risk subgroups in the early years after IIM diagnosis to improve cancer detection.

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Competing interests: none declared.

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