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Evidence supports blind screening for internal malignancy in dermatomyositis
Data from 2 large US dermatology cohorts

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Abstract
The association between dermatomyositis and internal malignancy is well established, but there is little consensus about the methods of cancer screening that should be utilized.

We wished to analyze the prevalence and yield of selected cancer screening modalities in patients with dermatomyositis.

We performed a retrospective analysis of 2 large US dermatomyositis cohorts comprising 400 patients.

We measured the frequency of selected screening tests used to search for malignancy. Patients with a biopsy-confirmed malignancy were identified. Prespecified clinical and laboratory factors were tested for association with malignancy. For each malignancy we identified the screening test(s) that led to diagnosis and classified these tests as either blind (not guided by suspicious sign/symptom) or triggered (by a suspicious sign or symptom).

Forty-eight patients (12.0% of total cohort) with 53 cancers were identified with dermatomyositis-associated malignancy. Twenty-one of these 53 cancers (40%) were diagnosed within 1 year of dermatomyositis symptom onset. In multivariate analysis, older age (P = .0005) was the only significant risk factor for internal malignancy. There was no significant difference in cancer incidence between classic and clinically amyopathic patients. Twenty-seven patients (6.8% of the total cohort) harbored an undiagnosed malignancy at the time of dermatomyositis diagnosis. The majority (59%) of these cancers were asymptomatic and computed tomography (CT) scans were the most common studies to reveal a cancer.

This is the largest US cohort studied to examine malignancy prevalence and screening practices in dermatomyositis patients. Our results demonstrate that, while undiagnosed malignancy is present in <10% of US patients at the time of dermatomyositis onset, it is often not associated with a suspicious sign or symptom. Our data suggest that effective malignancy screening of dermatomyositis patients often requires evaluation beyond a history, physical examination, and “age-appropriate” cancer screening—these data may help to inform future guidelines for malignancy screening in this population.

Abbreviations: ACS = American Cancer Society, CA 19–9 = cancer antigen 19–9, CA-125 = cancer antigen 125, CBC = complete blood count, CK = creatinine kinase, CT = computed tomography, DLBCL = diffuse large B-cell lymphoma, DM = dermatomyositis, EBV = Epstein Barr virus, EGD = esophagogastrroduodenoscopy, ESR = erythrocyte sedimentation rate, LDH = lactate dehydrogenase, PET = positron emission tomography, PSA = prostate specific antigen, US = United States, USPSTF = United State Preventative Services Task Force.

Keywords: connective tissue disease, dermatomyositis, malignancy, screening

1. Introduction
Dermatomyositis (DM) is a systemic autoimmune disease characterized by proximal muscle weakness and characteristic skin rash. The association between DM and internal malignancy has been well established,[1–4] although the frequency of underlying malignancy varies greatly (3–40%) between studies.[5] The mechanism of the relationship between DM and malignancy is unknown, but may include: increased risk of cancer in the setting of immunosuppressive therapy; increased detection
in the setting of heightened surveillance; DM occurring in the setting of an immunologic response to internal malignancy.

Complications secondary to underlying cancer are a leading cause of mortality in DM,\(^5\) and thus it follows that early identification of malignancy may allow for improved outcomes. Multiple clinical and laboratory features have been identified that are associated with underlying malignancy in DM\(^6\) such as age, sex, and autoantibody status, although it is currently not clear how these data should impact cancer screening in clinical practice.

Although it is generally accepted that DM patients should undergo some type of cancer screening, there is no consensus regarding the methods or frequency by which this should occur. Some authors have suggested that blind screening tests are not useful in an otherwise asymptomatic patient,\(^6\) while more recent work has supported the utility of a meticulous search at the time of diagnosis, including pan computed tomography (CT) scanning and endoscopic gastrointestinal studies.\(^5,7\) There are very limited data to provide guidance on this topic, and those that exist are difficult to interpret due to small patient numbers. We took advantage of 2 large US cohorts comprising 400 DM patients to retrospectively analyze the use and utility of selected malignancy screening modalities in diagnosing DM-associated malignancy. Our goal is to provide data that can inform the future development of evidence-based guidelines for cancer screening practices in DM patients.

2. Methods

We conducted a 2-site study that was approved by the Human Subjects Committees at both Stanford University and the University of Louisville. The charts of all patients with an ICD-9 diagnosis code of 710.1 (DM) that were followed by at least one of the authors between July 2002 and September 2013 (Stanford Department of Dermatology) or January 1983 and December 2013 (Louisville Department of Dermatology) were retrospectively reviewed. Patient records were reviewed to confirm the diagnosis of dermatomyositis using either the criteria of Bohan and Peter\(^8\) or, for clinically amyopathic patients, the proposed criteria of Ewler and Sontheimer.\(^9\) All clinically amyopathic patients had a skin biopsy consistent with DM. Clinically amyopathic patients were defined as those patients with classic DM skin lesions for at least 6 months with neither signs nor symptoms of muscle weakness nor elevated muscle enzymes. Information on all biopsy-proven malignancies (excluding non-melanoma skin cancer) was recorded, and those cancers (or cancer recurrences) diagnosed within 5 years (before or after) of the first DM-related symptom onset were defined as “associated” with DM. To analyze risk factors for cancer, various clinical features and/or laboratory values present at the time of DM diagnosis were recorded. Any of the following were considered potential cancer screening procedures, as long as they occurred at or following the date of DM diagnosis: circulating cancer antigens (CA-125, CA 19-9), prostate specific antigen (PSA), serum/urine protein electrophoresis, chest radiography, mammography, colonoscopy or sigmoidoscopy, esophagogastroduodenoscopy (EGD), computed tomography (including head/neck, chest, abdomen, or pelvis), pelvic ultrasound, and positron emission tomography (PET). Complete blood count, comprehensive chemistry, and urinalysis tests were also considered to be cancer screening tests if they were performed as part of the comprehensive workup for malignancy in light of dermatomyositis diagnosis. Due to incomplete documentation, we excluded fecal occult blood testing, Papanicolaou testing, LDH, and ESR values from the analysis. All tests were ordered at the discretion of the physician, and no prespecified guidelines were followed regarding cancer surveillance. Any potential cancer-screening test that ultimately led to a biopsy diagnosis of cancer was regarded as an “informative” test. Each cancer screening procedure was coded as either “blind” (performed in a patient without cancer-concerning symptoms, purely as a screening test given their diagnosis of DM) or “triggered” (performed to further evaluate a cancer-concerning sign or symptom).

3. Statistical analysis

Descriptive statistics were evaluated for demographic and clinical data in the total population as well as specifically in the patients identified as having a concurrent cancer during the ±5 year window. To maximize the use of available data and minimize potential bias in the setting of missing variables, multiple imputation was performed, including the use of regression for continuous variables and discriminant function for categorical variables. Univariate logistic analyses were performed, followed by multivariate analyses. For maximum CK and maximum aldolase levels, the data were not normally distributed; data were grouped into quartiles and presented results reflect the first versus fourth quartiles. All tests were 2-sided, and \(P\) values < .05 were considered significant. Analysis was performed using SAS Institute Inc. (Cary, NC, version 9.4).

4. Results

4.1. Cancer frequency and subtypes

Four hundred patients were identified with dermatomyositis, including 215 from the University of Louisville and 185 from the Stanford University Dermatology clinics. Patients had a median age of 51.9 years at diagnosis [interquartile range (IQR) 41.5–61.8 years] and were predominantly female (80.8%) and Caucasian (81.2%) (Table 1). Nearly, a quarter (23.5%) of the patients were clinically amyopathic. Patients were followed for a median time period of 4.2 years after symptom onset (IQR 1.7–8.6 years). We identified 74 total cancers in 63 patients (15.8% of 400 patients). The majority of the cancers diagnosed (53/74, or 72%) occurred within 5 years (before and after) of DM symptom onset, and thus were defined as being DM-associated (Fig. 1, see eTable 1 in the supplement, http://links.lww.com/MD/

| Table 1 | Baseline characteristics of DM patients. |
|---------|----------------------------------------|
| Variable | Total | Stanford | Louisville |
| Age at DM symptom onset (median, range) | 51.9 (6–87) | 48.4 (8–87) | 51.7 (18–86) |
| Male (n, %) | 77 (19.3%) | 47 (25.4%) | 30 (14.0%) |
| Race | | | |
| Caucasian (n, %) | 290 (81.2%) | 105 (63.6%) | 185 (96.3%) |
| Latino (n, %) | 25 (7.0%) | 25 (15.2%) | 0 (0%) |
| Asian (n, %) | 22 (6.2%) | 22 (13.3%) | 0 (0%) |
| African American (n, %) | 11 (3.1%) | 6 (3.6%) | 5 (2.6%) |
| Pacific Islander (n, %) | 9 (2.5%) | 7 (4.2%) | 2 (1.0%) |
| Length of follow up in years (median, range) | 4.2 (0.06–42.0) | 4.1 (0.06–39.6) | 4.3 (0.1–42.0) |
| Clinically amyopathic (n, %) | 90 (23.4%) | 36 (19.8%) | 54 (26.9%) |
| Interstitial lung disease (n, %) | 40 (11.4%) | 35 (23.3%) | 5 (2.5%) |

DM = dermatomyositis.
C77), Five patients had 2 separate cancers and thus 48 patients (12.0% of the total cohort) were identified as having cancer-associated DM (Fig. 1). 40% (21/53) of the DM-associated cancers were diagnosed within 1 year of onset of DM symptoms (Fig. 1). Three of the cases of DM-associated malignancy represented a cancer relapse that occurred during the 5-year window of their DM symptom onset, including recurrent acute lymphocytic leukemia, breast cancer, and recurrent metastatic breast cancer.

We identified a variety of types of cancers in the group of patients found to have a DM-associated malignancy; the most frequent included breast (13 cases, 24.5%), hematologic (9 cases, 17.0%), colorectal (5 cases, 9.4%), and prostate (5 cases, 9.4%) (eTable 1, http://links.lww.com/MD/C77). Five of the 9 hematologic malignancies were diagnosed following DM onset—of these, 4 were identified in patients already on immunosuppressive therapy (methotrexate, azathioprine, and/or mycophenolate mofetil) for their DM, prior to their cancer diagnosis. Of these 4 patients, 2 were diagnosed with EBV-associated lymphoma (gingival lymphoma and cutaneous diffuse large B cell lymphoma). As EBV-associated lymphomas occur mainly in the setting of immunosuppression, this suggests that at least some cancer cases were iatrogenic.[10]

4.2. Malignancy risk factors

We next investigated whether any clinical or laboratory risk factors present at the time of DM diagnosis were associated with malignancy. Older age was found to be significantly associated with malignancy ($P=.0001$) (Table 2). The average age at DM diagnosis in the cancer group was 58.0 years (range 24–87 years old), compared with an average age of 48.9 years (range 8–87) in patients without cancer-associated DM. The percentage of men was significantly higher in the cancer versus non-cancer group (OR 0.47, 95% CI 0.24–0.92; $P=.0271$). However, in a multivariate analysis, only age remained a significant risk factor associated with the presence of cancer (OR 1.04, 95% CI 1.02–1.06; $P=.0005$). There was no difference in cancer incidence between classic versus clinically amyopathic patients.

4.3. Cancer screening procedures and outcomes

We compared the frequency of cancer screening practices at each clinical site. Besides CBC and chemistry panels, the most frequently performed studies included CT scans (chest/abdomen/pelvis), mammography, chest radiography, and colonoscopy (see eTable 2 in the supplement, http://links.lww.com/MD/C77). The cancer screening practices at both sites were generally comparable (eTable 2, http://links.lww.com/MD/C77).

We next examined in more detail the events leading to a diagnosis of malignancy. Of the 53 DM-associated cancers, 24 were diagnosed before and 29 were diagnosed after DM onset (Fig. 2). This latter group of 29 cancers represents the number of occult cancers at the time of DM diagnosis, and occurred in 27 patients (6.8% of the original cohort of 400). Of these 29 cancers, 12 were ultimately diagnosed following tests that were performed to investigate a cancer-concerning suspicious element in the patient history and/or physical examination (e.g., “triggered” tests; Fig. 2). The factors that prompted a triggered test included hematuria, unintentional weight loss, melena, abdominal pain, postmenopausal bleeding, epistaxis with excessive phlegm production, and suspicious pigmented lesions or cutaneous nodules. In only 3 of these 12 cancers were the suspicious signs or symptoms present at the time of DM diagnosis. For the remaining 9 cases, deemed “late cancer symptom onset,” we investigated how many were the result of failure of appropriate blind screening practices. We had sufficient data to answer this question in 6 cases. Two female patients each had a single, negative pelvic ultrasound performed before eventual onset of vaginal bleeding and repeat pelvic ultrasound leading to
diagnosis of endometrial carcinoma; 1 patient did not receive a timely colonoscopy before eventual melena and colonoscopy leading to diagnosis of colon cancer; the remaining 3 cases were melanoma, cutaneous B cell lymphoma, and nasopharyngeal carcinoma, none of which would have been reasonably likely to be detected using any of the blind screening modalities discussed (other than a careful history and physical examination).

We next examined the group of 17 cancers that were diagnosed via purely blind screening examinations in patients with a non-concerning history and physical examination (Fig. 2). These latter cancers included 3 cases each of breast cancer, renal cell carcinoma, and colon cancer, 2 cases each of prostate cancer and lymphoma, and a single case of ovarian cancer, thyroid cancer, myelodysplastic syndrome, and lung cancer (Table 3). The most frequently informative tests were CT scanning and mammography, which led to a diagnosis for 35% and 18% of the asymptomatic cancers, respectively (Table 3). For the 6 cancers diagnosed following blind CT scans, none had prior ultrasound examination of the involved area.

We were interested in the yield of repeat blind screening tests following an initially negative evaluation. Two of the 17 cancers were identified on a blind, repeat screening test following a previously negative identical screening. In 1 patient, a repeat mammogram diagnosed breast cancer nearly 4 years after the onset of her DM symptoms, despite a negative mammogram 1 year prior. In the second patient, a repeat CT chest/abdomen/pelvis identified a new diffuse large B cell lymphoma after an initial pan-CT scan (1 year prior) had been negative; this malignancy was diagnosed nearly 3 years after initial onset of DM symptoms. These 2 cases are in addition to the 2 “false negative” pelvic ultrasound cases mentioned above.

5. Discussion

The relationship between DM and malignancy is well established, although the prevalence and types of cancers varies widely among the populations studied.\[^{3,11}\] In addition, most studies do not include or specifically consider clinically amyopathic patients.\[^{1,2,4,6}\] This study represents the largest dataset from the perspective of an outpatient dermatology setting in the United States. We found that 12% of DM patients had a malignancy diagnosis in the 5 years before or after DM symptom onset, encompassing 72% of all malignancies recorded in this population. We noted the highest frequency of diagnosis in the 1 year following DM symptom onset, which is consistent with previous reports.\[^{11}\] These data support the concept that onset of malignancy and DM are closely and temporally linked, although the mechanism of this association is still unclear. It is possible that, as with some cases of scleroderma, DM can be the secondary result of a dysregulated immune response to an initial cancer.\[^{12}\] However, other explanations exist for the link between cancer and DM, and it is possible that multiple mechanisms could

Table 2

| Variable                        | Odds ratio (95% confidence interval) | P-value |
|---------------------------------|--------------------------------------|---------|
| Age                             | 1.04 (1.02–1.06)                     | .0001   |
| Gender                          | 0.47 (0.24–0.92)                     | .0271   |
| Race                            |                                      |         |
| Caucasian                       | 0.46 (0.09–2.27)                     | .3381   |
| African American                | 0.39 (0.03–5.20)                     | .4755   |
| Asian                           | 1.03 (0.16–6.59)                     | .974    |
| Latino                          | 0.90 (0.14–5.73)                     | .9145   |
| ILD                             | 0.96 (0.58–1.58)                     | .8707   |
| Clinically amyopathic           | 1.04 (0.73–1.47)                     | .8361   |
| Dysphagia                       | 1.09 (0.79–1.51)                     | .5886   |
| Dysphonia                       | 1.23 (0.83–1.83)                     | .2987   |
| Anthralgia                      | 1.02 (0.73–1.43)                     | .8942   |
| Raynaud’s                       | 0.87 (0.52–1.44)                     | .5756   |
| Smoking history                 |                                      |         |
| Non-smoker vs current           | 0.58 (0.21–1.62)                     | .2995   |
| Prior smoker vs current         | 0.60 (0.16–2.26)                     | .4515   |
| Maximum CK                      | 0.60 (0.24–1.53)                     | .2872   |
| Maximum aldolase                | 1.34 (0.50–3.59)                     | .5623   |
| Albumin                         | 0.63 (0.37–1.07)                     | .0867   |
| Univariate analysis             |                                      |         |
| Age                             | 1.04 (1.02–1.06)                     | .0005   |
| Gender                          | 0.74 (0.45–1.20)                     | .0988   |
| Albumin                         | 0.76 (0.44–1.33)                     | .341    |

Maximum aldolase and CK values were divided into quartiles; the data presented reflect first versus fourth quartiles but similar results were found for other quartile comparisons. CK= creatine kinase, DM= dermatomyositis, ILD= interstitial lung disease.

Figure 2. Flowchart for cancer diagnoses. DM associated malignancy is any cancer occurring within 5 years of DM diagnosis. Malignancies occurring after DM onset were considered to be diagnosed in 1 of 2 ways: following screening tests performed in response to a suspicious element in the patient’s history or physical exam (TRIGGERED) or following screening tests performed for no other reason except for a DM diagnosis (BLIND). DM=dermatomyositis.
underlie this association—for example, 2 of our patients had EBV-related B cell lymphoma, which suggests that immunosuppressive therapy for the DM may play a role in some cases.

Regardless of mechanism, clinicians still are left with difficult questions regarding whom and how to screen for malignancy amongst the DM population. As for whom to screen, a recent meta analysis concluded that several factors are associated with both increased cancer risk (male sex, older age, dysphagia, cutaneous necrosis, rapid onset myositis, cutaneous vasculitis, high ESR) and decreased cancer risk (interstitial lung disease, arthralgia, Raynaud’s). Out results confirmed increased cancer risk with older age although this effect was modest. We were not able to show an association of cancer with male sex or dysphagia, although our study is of modest size and retrospective in nature.

We did not evaluate for cutaneous necrosis, vasculitis, or tempo of disease onset in this study. Finally, recent data suggest that certain DM-associated autoantibodies might impact cancer risk,[13] but we did not evaluate these systematically in our cohort. It remains to be seen how any of these clinical factors should be used to quantitatively direct clinicians regarding who receives intensive cancer screening.

Since the first description of clinically amyopathic DM, it has long been questioned if this group of patients has a similar increased cancer risk as their classic DM counterparts. To date, this association has only been described in case reports and small patient series. A meta-analysis suggested that these patients are likely also at increased cancer risk.[14] Our study is the largest to date to evaluate the prevalence of internal malignancy in the CADM group, and we find that there is no statistical difference in cancer risk between CADM and classic DM patients. Thus, our data support that clinically amyopathic DM patients deserve the same consideration for cancer screening as their classic counterparts.

In light of these data, the clinician needs to consider the possibility of malignancy in all recently diagnosed DM patients. The question of which modalities are of highest yield for cancer screening in the DM population is of high priority. Rational screening guidelines should be based on real data in this population—unfortunately, most large studies of DM populations do not provide data regarding the method by which malignancies were ultimately detected. Most authorities would recommend a thorough history and physical examination in this population, which is not necessarily based on data but on common sense and a desire for cost effectiveness. Our data show that, in patients with a recent diagnosis of DM without a known cancer, a significant portion (41%) of the cancers that were ultimately diagnosed were associated with a suspicious sign or symptom. These symptoms included unintentional weight loss, melena, postmenopausal bleeding, epistaxis, persistent abdominal pain, and abnormal skin examination findings, including cutaneous nodules or pigmented lesions. In addition, 3 cancers were diagnosed following unexplained leukocytosis, anemia, or microscopic hematuria, supporting (at least) the use of a complete blood count and urinalysis for screening purposes.

It would also seem reasonable that any DM patient should be up to date regarding age-appropriate guidelines for cancer screening from the American Cancer Society (ACS) and/or US Preventive Services Task Force (USPSTF).[15] However, in our group of 17 cancers diagnosed using blind screening tests, only 5 would have been considered “appropriate” as dictated by guidelines for cancer screening in an otherwise healthy adult per the recommendations of the ACS, and only 3 would have been recommended by the USPSTF (Table 3). Our data demonstrate the utility of colonoscopies, as 2 patients were diagnosed with blind studies (Table 3) and, given its size, a third cancer would have likely been discovered had a timely colonoscopy been performed (see Results). Mammograms also were informative, although 2 patients with breast cancer (discovered with a mammogram) were outside the USPSTF age guidelines for screening mammography (age 48 and 86; Table 3). Additionally, we diagnosed 2 of our male patients on the basis of an abnormal PSA. The ACS recommends that men be given the opportunity to make an informed decision with their physician about the use of this screening exam, while the USPSTF recommends against screening with a PSA. If we include the PSA as an “age-appropriate” screening examination, and utilize the CBC and urinalysis panel screens discussed above, our cohort still would have had 8 cancers (47%) go undetected. These data suggest that following “age appropriate” guidelines may not be aggressive enough screening in the DM population, possibly due to the fact that the pretest probability of cancer is higher than the general population.

Given the lack of sensitivity of traditional cancer screening modalities in the DM population, what other test(s) should be performed? In our study, we found that a CT chest, abdomen, pelvis was particularly high yield, leading to a cancer diagnosis in 6 of the 8 remaining malignancies for which we have clear data on the testing that led to cancer diagnosis. Our data are consistent with a previous small study that supported the use of a meticulous cancer screen at the time of DM onset.[16] This retrospective study looking at 40 patients with dermatomyositis and polymyositis, 13 of 33 DM patients were diagnosed with malignancy. The authors noted that 54% of their directed screening exams yielded positive results, while 13% of blind studies were informative; the highest yield blind studies were chest and pelvic CT scans. Although we also found the CT scan to be of high yield, we are not able to state that these cancers would not have been discoverable using other, less expensive modalities such as ultrasound with or without a pap smear. However, given the location of these tumors, this would have required ultrasound over several regions (e.g., thyroid, kidney, pelvic) and it is unclear whether some of these small tumors would have been detected by ultrasound. In addition, it is interesting to note that 2 endometrial carcinoma cases were diagnosed following negative pelvic ultrasound studies the year before. Finally, while we did not specifically address the utility of PET/CT screening in our cohort, a recent study examined the potential utility of this modality.[17]
for cancer screening in DM. This study of 55 patients with DM and polymyositis found that the use of PET/CT scanning was comparable to conventional screening practices (similar to the methods described above, including the use of thoracoabdominal CT scanning), but the utility of this method needs to be clarified in larger studies.\textsuperscript{[11,12]} We realize that cost considerations will need to be factored in to any future guidelines on malignancy screening, and the purpose of this study was not to be a final recommendation on which screening modalities should be used. However, our data suggest that use of imaging modalities beyond “age appropriate” cancer screening testing is warranted in the DM population.

Another important issue is the role for repeat blind cancer screening in DM patients. We found that, in our cohort, 2 patients were diagnosed as the result of a repeated screening study, including a blind repeat mammogram diagnosing breast cancer and a blind repeat CT scan diagnosing retroperitoneal DLBCL. In addition, 2 patients had negative pelvic ultrasounds followed by eventual diagnosis of endometrial carcinoma over a year later, bringing up the possibility that repeat screening might have detected these before they became symptomatic. Thus, our data suggest that repeat screening may identify cancers that are not initially detected with blind screening, although it is unclear at present who deserves such screening.

Our study has several limitations. First, it is a retrospective analysis, and thus we are limited in our ability to evaluate all potential cancer screening modalities and potential risk factors associated with cancer. For instance, due to incomplete data we were unable to include Papanicolaou testing or stool guaiac studies. In addition, our physicians did not follow a standardized method for systematically screening patients for cancer, and thus we are not able to give precise sensitivity and specificity data for each of the screening tests. It is possible that other modalities might have detected some of the cancers that were found by CT examination, including those that are less expensive or do not expose the patient to radiation, but we are only able to present the results of our screening practices. Our study does not attempt to take into account cost effectiveness issues and we have no evidence that early detection of cancers using more aggressive screening practices such as CT scans actually improves patient outcomes or reduces mortality. Additionally, the median length of follow up is relatively short (4.2 years), making it possible that some DM-associated malignancy cases were not identified, although this is likely a small number. Despite this, our data suggest that DM patients should be screened for cancer more aggressively that traditional guidelines recommend.

6. Conclusions

We show that in our large cohort of outpatient dermatology clinic patients in the United States that approximately 12% of patients have an associated internal malignancy in both the clinically amyopathic and classic DM patients. A reasonable algorithm for cancer screening starts but does not end with a history and physical exam, complete blood count, urinalysis, consideration for yearly mammograms in women of all ages in addition to other age-appropriate screening guidelines. It appears that other modalities, such as CT scans but possibly others, are indicated in order to detect the majority of latent malignancies in the DM population. Future studies will be needed to identify how clinical and laboratory risk factors might impact these general screening practices, as well as how often they should be repeated in the DM population.

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