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Patient Characteristics, Diagnostic Journey, and Cancer Enrichment Among Patients with Nonspecific Signs and/or Symptoms in the US Community Oncology Setting: A Real-world Retrospective Study

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INTRODUCTION

- Of the ~1.8 million people diagnosed with cancer in the US each year,[1] >60% are diagnosed after symptomatic presentation, including presentation with nonspecific signs and/or symptoms (NSSS)[2]
- NSSS, such as weight loss, anemia, fatigue, and pain, could be associated with a range of cancer or noncancer diagnoses and therefore may lack a clear diagnostic evaluation pathway[3]
- These NSSS may cause patients with cancer to undergo undirected or misdirected diagnostic evaluation while the possibility of cancer and search for its origin is explored, causing delayed treatment and poor outcomes[4-6]
- On the other hand, patients who do not have cancer are often subjected to various unnecessary procedures due to initial cancer suspicion

OBJECTIVE

- We used data from The US Oncology Network (The Network) to examine characteristics, diagnostic journey, and cancer incidence of patients with NSSS with the objective of understanding the unmet need for improved diagnostic processes and tools for cancer evaluation in patients with NSSS

METHODS

Data Source

- Structured data among patients within The Network was extracted from the iKnowMed (iKM) electronic health records (EHR) and the Financial Database Warehouse (The Network's repository of healthcare claims submitted by practices in The Network)

Study Cohort

- This retrospective observational cohort study included patients aged ≥40 with ≥1 of the following NSSS in their problem list at their first visit within The Network (index date) during the identification period from 1/1/2016 to 12/31/2020:
  - anemia, venous thromboembolism (VTE), general malaise, weight loss, nonspecific abdominal symptoms, new and unexplained breathlessness, unexplained worsening pain (especially back), abnormal lab test results, abnormal liver function test (LFT), abnormal coagulation profile, abnormal iron, and abnormal platelet or white blood cell (WBC) count
- Patients were excluded if diagnosed with any cancer (except basal cell carcinoma and squamous cell carcinoma skin cancer) within 3 years prior to or on index date

Outcomes and Statistical Analysis

- Patients were followed longitudinally with data from EHRs for initial cancer diagnosis, new noncancer diagnosis, death, until the end of study observation period (12/31/2021), or end of diagnostic evaluation period (at 12 months), whichever occurred first
- Demographic and clinical characteristics were assessed descriptively

KEY RESULTS: THERE IS AN UNMET NEED FOR DIAGNOSTIC DECISION SUPPORT TO AID IN ACHIEVING MORE TIMELY AND COST-EFFECTIVE MANAGEMENT OF PATIENTS WITH NSSS

Patient Disposition

- A total of 103,984 patients were eligible for inclusion (**Table 1**)

Table 1. Patient Attrition

Inclusion/exclusion criteria	Patients remaining
Patients with ≥1 NSSS from their problem list with a visit within The Network during identification period between 1/1/2016–12/31/2020	251,704
Above visit is their first visit for NSSS between 1/1/2016–12/31/2020	232,559
Patients ≥40 years of age at index date	201,163
Patients ≥1 additional vital visit within 12 months after the index date	170,874
Exclude patients with a documented diagnosis of any cancer (excluding basal cell carcinoma and squamous cell carcinoma skin cancer) in iKM within 3 years on or prior to index date	104,002
Exclude patients with inconsistent data	**103,984**

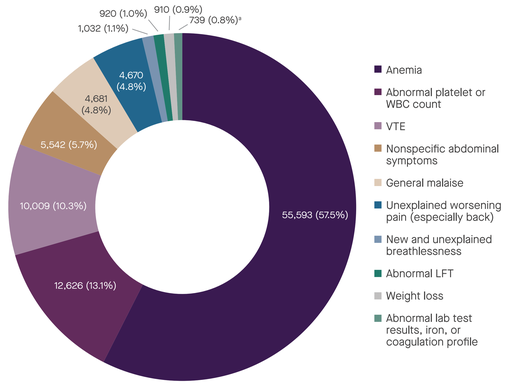
Patient Demographics

- Mean age was 64.9 ± 13.4 years
  - 53,875 (51.8%) patients were aged ≥65 years
- A total of 67,004 (64.4%) patients were female, 67,154 (64.6%) were White, 48,321 (46.5%) were never smokers, 42,099 (40.5%) were obese (BMI≥30), and 50,115 (48.2%) were from a southern practice region in the US
- Mean follow-up time from the index date until date of death, last visit, or end of the study observation period, whichever occurred first, was 20.0 ± 17.7 months
- A majority of patients (73%) were seen by a hematologist/medical oncologist during the study observation period

Clinical Characteristics

- Among patients with only 1 presenting NSSS category at index date (n=96,722), the most common (in ≥10% of patients) presenting NSSS were anemia, abnormal platelet or WBC count, and VTE (**Figure 1**)

Figure 1. Presenting NSSS Distribution



[a]Abnormal lab test results, 537 (0.6%); abnormal iron, 149 (0.2%); abnormal coagulation profile, 53 (0.1%).

Clinical Outcomes

- A total of 6,774 (6.5%) patients were diagnosed with cancer
  - Among patients diagnosed with 1 primary cancer (n=6,537), 3,825 (58.5%) were diagnosed with a primary hematologic malignancy and 2,712 (41.5%) with a solid tumor (**Table 2**)
- A total of 38,718 (37.2%) patients were diagnosed with ≥1 noncancer condition
  - The most common (in ≥10% of patients) noncancer conditions in patients diagnosed with only 1 noncancer condition (n=28,955) were:
    - blood and blood-forming organ diseases and certain disorders involving the immune mechanism (18,134 [62.6%] patients), circulatory system diseases (6,413 [22.1%]), endocrine, nutritional, and metabolic diseases (5,326 [18.4%]), and musculoskeletal system and connective tissue diseases (2,971 [10.3%])
- A total of 58,492 (56.3%) patients did not have any documented diagnoses

Table 2. Distribution of Primary Cancer Diagnoses

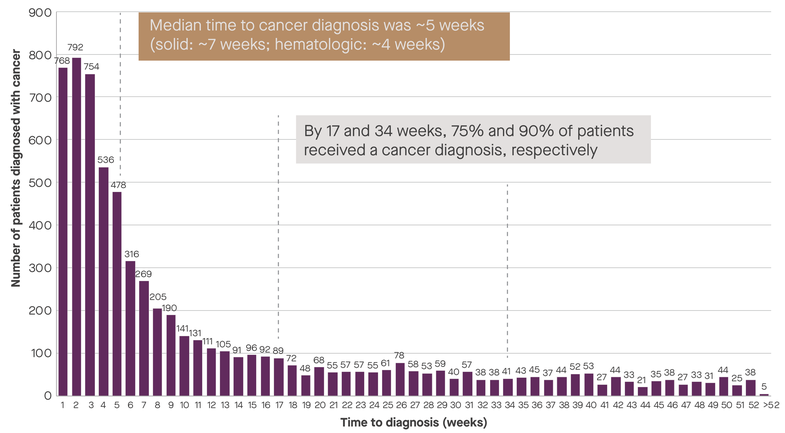
	Patients diagnosed with 1 primary cancer (n=6,537)
Primary hematologic malignancy, n (%)	**3,825 (58.5)**
Myeloid neoplasm[a]	1,911 (28.2)
Lymphoma	1,147 (16.9)
Plasma cell neoplasm	678 (10)
Lymphoid leukemia	89 (1.3)
Primary solid tumor, n (%)	**2,712 (41.5)**
Lower gastrointestinal	470 (7.2)
Genitourinary	412 (6.3)
Respiratory	395 (6.0)
Upper gastrointestinal	373 (5.7)
Breast	350 (5.4)
Other[b]	301 (4.6)
Gynecologic	296 (4.5)
Melanoma	66 (1.0)
Head and Neck	49 (0.7)

[a]Acute myeloid leukemia or chronic myeloid leukemia.
[b]Other category includes endocrine, neuroendocrine, neurologic, sarcoma, thyroid, non-melanoma skin cancer, other (unclassified), and unknown primary.

Time to Diagnosis

- Among patients diagnosed with cancer (n=6,774), median time from first visit within The Network with NSSS to new cancer diagnosis was ~5 weeks (solid: ~7 weeks; hematologic: ~4 weeks) (**Figure 2**)
  - By 17 and 34 weeks, 5,164 (76.2%) and 6,099 (90.0%) patients with cancer received their diagnosis, respectively
- Among patients diagnosed with only 1 noncancer condition (n=28,955) and >1 noncancer condition (n=9,763), 23,509 (81.2%) and 8,253 (84.5%) patients received a noncancer diagnosis, respectively, within 1 week

Figure 2. Time From First Visit to New Cancer Diagnosis Within The Network



LIMITATIONS

- There may be additional NSSS that may not have explicitly been captured in The Network iKM EHR
- Time to diagnosis was measured from the first secondary care visit instead of first primary care physician visit to final diagnosis and, thus, is not an accurate reflection of total time to diagnosis associated with NSSS
- This study defined the end of the diagnostic evaluation period as 12 months; thus, any diagnoses 12 months after the index date were excluded from our analysis
- We have limited capacity to differentiate between new cancer diagnoses and cancer recurrences diagnosed more than 3 years prior to the index date
- The retrospective nature of the study design precludes us from making robust associations between NSSS and diagnoses

CONCLUSIONS

- In conclusion, NSSS are associated with a range of cancer and noncancer diagnoses
  - Notably, a substantial proportion of patients (~40%) within this population of patients primarily seen by a hematologist/medical oncologist and with a cancer diagnosis were ultimately diagnosed with solid tumors within 1 year
  - It may be inferred that NSSS require advanced clinical consideration and decision making to achieve an accurate diagnosis and reduce the risk of an extended diagnostic evaluation period and potential harm from undirected or misdirected diagnostic procedures
- Time to cancer diagnosis from the secondary care setting in this study (~5 weeks) was lower than what it would be if it were measured from the first primary care visit for NSSS
  - However, ~25% and ~10% of patients still required >17 and >34 weeks to reach diagnosis, respectively
  - There remains a need for more efficient diagnostic evaluation pathways for NSSS in upstream care settings
- Our results highlight the unmet need for diagnostic decision support to aid in achieving more timely and cost-effective management of patients with NSSS
  - One potential approach is a multi-cancer detection test that could help in stratifying risk for cancer and direct diagnostic evaluation in patients with NSSS
  - Such a test could potentially improve outcomes, such as survival and quality of life, in patients with cancer while avoiding costly and potentially invasive misdirected testing in the remaining majority

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Disclosures

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