Understanding Barriers in the Pathway to Diagnosis of Ankylosing Spondylitis: Results From a US Survey of 1690 Physicians From 10 Specialties

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Objective. Early diagnosis of ankylosing spondylitis (AS) remains challenging because of the high prevalence of chronic back pain in patients initially treated by nonrheumatology health care providers (HCPs). We assessed the patient pathway to rheumatology referral, including HCP recognition of inflammatory back pain (IBP) and other features suggestive of AS, diagnostic workup, treatment, and referral to a specialist with the goal of identifying barriers to patient referral to a rheumatologist.

Methods. US HCPs from 10 specialties were invited to participate in a cross-sectional web-based survey on clinical characteristics and diagnostic measures leading to IBP suspicion and the subsequent referral process. Eligible HCPs were actively practicing and had referred a patient with suspected IBP or ocular findings (ophthalmology only) within 12 months. Data were analyzed descriptively.

Results. Of 1690 HCPs, 61% identified morning stiffness lasting more than 30 minutes, 29% sleep disturbance due to back pain, and 28% pain that improves with activity as features suggestive of IBP. Nearly two-thirds of primary care HCPs reported that they were the first HCPs consulted by patients with suspected IBP. Among HCPs ordering diagnostic blood work, approximately 90% selected antinuclear antibody and rheumatoid factor, whereas 76% selected human leukocyte antigen B27. Almost 40% would treat patients with suspected IBP themselves. HCPs cited lack of adequate specialists nearby (35.1%), insurance restrictions (47.1%), and long wait time (77.0%) as barriers to early referral.

Conclusion. Most HCPs had difficulty identifying features suggestive of IBP and indicated insurance restrictions and long wait times as barriers to early referral of patients with potential AS.

INTRODUCTION

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Ankylosing spondylitis (AS), a prototypical form of axial spondyloarthritis affecting 0.2% to 0.5% of the population in the United States (1), is one of the many causes of chronic back pain. The distinguishing pattern of back pain in AS is inflammatory back pain (IBP), which has an estimated prevalence of 5% to 6% among patients with chronic back pain in the United States (2–4). IBP is characterized by an insidious onset, duration of pain of more than 3 months, improvement of pain with exercise, pain at night with improvement upon waking, and no improvement with rest (5).

Diagnosis of AS is often delayed; in the United States, a delay in AS diagnosis of up to 13 years after symptom onset has been reported (6). The delay in diagnosis can complicate

disease management and contributes to significant patient burden, including pain, stiffness, fatigue, progressive loss of mobility and spinal function, and reduced quality of life (7–9). Patients with chronic back pain are frequently treated by nonrheumatology health care providers (HCPs), including primary care physicians, orthopedists, physiatrists, and chiropractors, in an attempt to relieve symptoms (6). The high prevalence of chronic back pain with the lack of specific physical examination findings and biomarkers in addition to good response to nonsteroidal antiinflammatory drugs (NSAIDs) in patients with AS limit prompt and adequate referral and subsequently contribute to delays in diagnosis (6). Moreover, there are no well-established screening tools for referral of patients with chronic back pain suggestive of AS. IBP has been used as a key component of all of the screening

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tools for AS, and the relatively high sensitivity of IBP for AS in at-risk patients (74%–81%) makes it useful for screening for AS (10). Early diagnosis and subsequent treatment of AS may substantively decrease the burden of disease for patients with AS and increase their quality of life.

In this survey of HCPs in the United States, we sought to assess the patient pathway to rheumatology referral and AS diagnosis, including recognition of symptoms of IBP and other features suggestive of AS in patients with chronic back pain, disease evaluation, approaches to treatment, and specialist referral. Our aim was to identify barriers to rheumatology referral among patients with putative IBP.

MATERIALS AND METHODS

Study design and setting. This was a two-phase observational study (Figure 1). The first phase consisted of qualitative research for the development of the questionnaire. Survey content was first generated based on concept elicitation interviews with three HCPs (one pain specialist, one ophthalmologist, and one primary care physician) who were asked open-ended questions about clinical features of IBP suggestive of rheumatic disease, circumstances that would lead them to suspect IBP, diagnostic workup to investigate rheumatic disease, and finally, the referral process to a specialist (Supplementary Table S1). HCPs were recruited by Survey Sampling International (SSI) for concept elicitation and interviewed via telephone for an hour each. The concepts derived from these interviews were then used to generate a draft questionnaire to assess HCP knowledge on the clinical characteristics of IBP suggestive of rheumatic disease, followed by the diagnostic workup undertaken and their perspectives on the referral process. Based on the concept elicitation interviews, it was determined that nonrheumatology HCPs were more familiar with "ankylosing spondylitis" than "axial spondyloarthritis"; therefore, "ankylosing spondylitis" was used in the survey.

The questionnaire was cognitively tested with 10 HCPs (1 HCP each from family medicine, internal medicine, dermatology, gastroenterology, ophthal as determined that nonrheumatology HCPs were mology, orthopedics, chiropractic, pain management, physical therapy, and physiatry), also recruited by SSI. Cognitive testing was intended to evaluate the questionnaire for clarity and to determine if respondents were able to interpret the questions and formulate their responses easily and consistently. To ensure that each HCP was able to ultimately consider patients who either had IBP or an autoimmune rheumatic disease (ARD) according to their specialty, the initial questions were differentiated for each specialty for relevance, as appropriate. After the initial triage guestions were asked, the remainder of the survey questions were differentiated only for ophthalmologists. The phrase "inflammatory back pain" was ultimately used in the questionnaire for all specialties except ophthalmologists. Ophthalmologists were asked about patients who may have ocular findings suggestive of ARD.



Figure 1. Study design and data analysis. Abbreviation: HCP, healthcare provider. [Color figure can be viewed at wileyonlinelibrary. com]

From here, we use the phrase "inflammatory back pain" or "IBP" throughout the remainder of the manuscript to encompass all of these conditions. Based on the feedback received during cognitive testing, the questionnaire was revised and finalized (Supplementary Appendix).

The final questionnaire was composed of multiple sections, including an HCP demographic section comprising questions about their practice (medical degree, practice setting [urban vs rural practice], sector of practice [private vs public], and practice type [solo vs group]). Subsequent sections asked HCPs to answer questions regarding key steps in the pathway of evaluating patients with chronic back pain (i.e., their knowledge and recognition of patient symptoms suggestive of IBP, the diagnostic process once IBP is suspected, approaches to treatment, and barriers to specialist referral). The final section focused on what the providers considered essential teaching modalities to improve their knowledge about diagnosis and treatment of AS.

The second phase of the study comprised a cross-sectional web-based survey of HCPs who had previously referred a patient

with suspected IBP to a specialist. HCPs from all 10 specialties were invited to participate in the web survey. HCPs were recruited by SSI between June 27, 2018 and July 20, 2018. HCPs who were currently licensed, actively practicing in the United States, and had referred a patient with suspected IBP (except ophthalmology) or with ocular findings suggestive of ARD (ophthalmology only) within the past 12 months were eligible to participate. Survey invitations were emailed to HCPs and included a unique survey link and an embedded password for accessing the survey, as well as a unique random-user identification number that was used to ensure that each eligible participant completed the guestionnaire only once. Self-reported eligibility was confirmed via a screener module of the survey, which was completed before the participants were considered eligible for the full survey. Informed consent was obtained electronically after screening. Once HCPs were deemed eligible and provided informed consent, they were able to access the survey. The web-based survey was self-administered, and HCPs could complete it at their convenience. HCPs in both phases of our study were compensated in accordance with industry practice and standards.

RTI Health Solutions (RTI-HS) was responsible for questionnaire development and review, online survey programming, hosting, testing and quality control, oversight of data collection and field update summaries, as well as review and quality control of data files and deliverables. SSI was responsible for recruiting HCPs using unique links provided by RTI-HS. Participants for this study were recruited into the panel through many channels, including partnerships with trusted loyalty programs, online banner advertisements, TV advertising, emails, apps, social media influencers, websites, and offline methods. HCPs were recruited from SSI's physician panel. SSI maintains relationships with large numbers of physicians via panels to enable ready access to sampling pools for purposes of quantitative and qualitative research.

Physician data were entered directly into the Qualtrics webbased survey platform, hosted by RTI-HS. Contactable personal identifiers (including email addresses and IP addresses) collected for the study were not stored with physician data, and study data were deidentified and removed prior to exporting for analysis.

Study variables and data analysis. Data regarding patient symptoms and presentation, patient evaluation process, and patient referral process were collected from participating HCPs. Data were analyzed using descriptive statistics. For continuous variables, the mean, SD, median, interquartile range, and range are presented. Frequencies and percentages are reported for categorical data. No imputation of item-level missing data was planned for this study. The sample size is reported for each variable. Data for each question are summarized by specialty and overall. The analysis population consisted of HCPs who were eligible for the study and provided informed consent. HCPs ranking of referral attributes and educational materials by importance were analyzed by question using the surface under the cumulative

ranking (SUCRA) curve, a simple numerical summary expressed by a percentage that describes an overall ranking of a choice among available choices being ranked; its values range between 0% and 100% (11). A value of 100% would indicate that the respective choice was unanimously ranked most important and a value of 0% would indicate that the respective choice was unanimously ranked least important by HCPs. A higher SUCRA value indicates a higher likelihood that a particular referral attribute or educational material was chosen by HCPs to be of higher rank in relation to other items being rated.

RESULTS

HCP demographics. Of 2395 HCPs screened, 1690 were eligible and consented to be included in our study. Participating HCPs had been in practice for a mean (SD) of 16.0 (10.0) years. Approximately half (47.8%) reported practicing in a private group practice, 18.5% in an academic/hospital setting, 16.0% in a community hospital/clinic, and 14.6% in a private solo practice; 50.2% of participating HCPs practiced in a suburban setting. Additional information of HCP demographics by specialty is provided in Table 1.

Patient symptoms and presentations. Overall, HCPs saw a median of 100 patients with chronic back pain, including a median of 12 patients with suspected IBP, within the past 12 months of the survey (Figure 2A). Approximately half of HCPs (54% [range, 43%–66%]) selected age as a factor that would influence their suspicion of IBP. HCPs most commonly reported an average time of 1 to 2 months (17.5%), 3 to 4 months (18.2%), or 1 to 2 years (17.1%) after the onset of symptoms before a patient decided to consult them. Overall, 34.8% of HCPs reported that they were the first HCP their patients consulted after experiencing symptoms; of the 778 HCPs (46%) who reported that their patients had seen one or more specialists before them, 57.2% reported that their patients had seen two or more prior HCPs (Figure 2B). However, 62.8% of primary care HCPs indicated that they were the first HCPs that patients had consulted. In contrast, only 18.7% and 20.2% of chiropractors and physical therapists, respectively, were the first HCPs seen by their patients.

Generally, varied responses were noted among HCP specialties for symptoms and presentations indicative of IBP (Figure 3). The majority of HCPs (44.1%–72.0%) in all specialties indicated that more than 30 minutes of morning stiffness would lead them to suspect IBP. Overall, approximately one-third of HCPs (27.3%– 42.7%) reported their suspicion of IBP in patients with chronic back pain that improved with NSAID therapy. Up to one-third of HCPs (18.1%–35.3%) considered pain that gets better with activity as suggestive of IBP. Only 16.3% of the providers recognized alternating buttock pain as a feature of IBP. The majority of HCPs indicated that the presence of inflammatory bowel disease (62.9%) or psoriasis (55.6%) would lead them to suspect IBP.

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Figure 2. (A) Median number of patients presenting relevant chronic back pain symptoms compared with patients with suspected IBP seen by HCPs within the past 12 months. (B) The proportion of treating HCPs indicating that they were the first provider seen by patients with suspected IBP. The "physiatrist" specialty category includes physiatrists, rehabilitation specialists, and physical medicine practitioners. HCPs in all specialties except ophthalmology were asked to respond "yes," "no," or "not sure" to the question "Typically, do your patients who experience symptoms that may be related to inflammatory back pain see other specialists before coming to see you?" Ophthalmologists were asked "Typically, do your patients who experience symptoms that may be related to an autoimmune rheumatic disease see other specialists before coming to see you?" Abbreviations: HCP, healthcare provider; IBP, inflammatory back pain. [Color figure can be viewed at wileyonlinelibrary. com]

Once IBP was suspected, HCPs elected to perform further diagnostic workup for specific inflammatory diseases (74.3%), order diagnostic imaging (67.6%) or blood work (61.7%), refer the patient directly to another physician (57.3%), treat the patients to alleviate pain (49.3%), and treat the patients themselves (39.6%). With regard to imaging tests, the majority of HCPs (92.4%) opted for x-ray of the pelvis or spine and 66.4% opted for magnetic resonance imaging of the pelvis or spine (Figure 4A). Approximately 90% of HCPs elected to test for C-reactive protein, erythrocyte sedimentation rate, antinuclear antibodies (ANA), complete blood count, and rheumatoid factor (RF), whereas 75.5% selected human leukocyte antigen (HLA)-B27, 72.9% a

comprehensive metabolic panel, 44.7% citrullinated peptide antibody, and 27.2% fasting glucose (Figure 4B). Of the 669 HCPs who indicated that they would treat patients with suspected IBP themselves, 81.4% would recommend physical therapy, 79.1% would recommend NSAIDs, 40.4% would recommend opioids, 36.2% would recommend biologic therapy, and 38.9% would recommend disease-modifying antirheumatic drugs (Figure 4C).

Patient referral process. Of the 740 HCPs who indicated they would refer patients with suspected IBP to another specialist, 76.4% would refer to a rheumatologist. Overall, only 220 of 1689 HCPs (13.0%) would refer patients with suspected IBP to another



Figure 3. Select patient symptoms or presentations that led HCPs to suspect IBP. The "physiatrist" specialty category includes physiatrists, rehabilitation specialists, and physical medicine practitioners. Abbreviations: HCP, healthcare provider; IBP, inflammatory back pain. [Color figure can be viewed at wileyonlinelibrary.com]

specialist without any further diagnostic workup or initial treatment (Figure 5A). Upon referral, 90.2% of HCPs estimated a wait time of up to 2 months for their patient to see another specialist. HCPs reported that their patients identified long waiting times and insurance restrictions as the two primary reasons preventing their patients from being able to see a specialist right away (Figure 5B).

HCPs were asked to rank the following attributes by order of importance when deciding to refer patients to a specialist: accessibility (distance, waiting times), patient rapport and ease of communication with a specialist, specialist's expertise in treating autoimmune disease, and insurance coverage. Overall, specialist's expertise was ranked as the most important attribute (SUCRA, 80.0%), followed by accessibility (42.4%), insurance (40.5%), and patient rapport/ease of communication (37.2%) (Figure 5C).

Additional educational needs to enhance knowledge on rheumatologic conditions. HCPs provided their perspectives regarding educational means or materials that would be helpful for them to better recognize symptoms of IBP to improve their knowledge of rheumatologic conditions and referral practices. Overall, 62.3% wanted to learn about the clinical course of disease, 58.8% wanted more information on clinical evaluations, and 50.3% indicated that education about new and emerging treatments would be helpful. Additionally, they were asked to rank the most important educational means and/ or materials; expert guidelines on diagnosis and treatment was ranked as most important overall (SUCRA, 62.1%), and no clear differentiation was noted between this and the other educational materials (Figure 6).

DISCUSSION

Our survey of 1690 HCPs in the United States indicated that most surveyed practitioners had difficulty identifying the characteristic features of IBP in patients with chronic back pain. The most commonly recognized feature of IBP was morning stiffness lasting longer than 30 minutes. However, only one-third of the providers were able to relate back pain that gets better with activity, the parameter with the highest sensitivity for the diagnosis of AS, with IBP. Additionally, alternating buttock pain, which has a low sensitivity but high specificity for AS, was recognized by only 16% of HCPs as a feature of IBP. In contrast, the majority of HCPs overall indicated that the presence of inflammatory bowel disease or psoriasis would lead them to suspect IBP in patients with chronic back pain. Although insidious onset of back pain before the age of 45 is characteristic of IBP (5), only 54% of HCPs overall selected age as an important indicator of potential IBP. IBP has been an effective selection criterion in primary care of patients presenting with chronic back pain for referral to a rheumatologist (10). The lack of recognition of IBP criteria by the surveyed physicians may contribute to delay in referral and timely diagnosis of AS.

Nearly 90% of the surveyed HCPs selected RF and ANA as the initial diagnostic tests in patients suspected to have IBP to confirm the presence of ARD. This suggests a widespread use of these tests despite the low pretest probability of rheumatoid arthritis and systemic lupus erythematosus in patients with IBP suggestive of AS. To reduce unnecessary medical testing, the American Board of Internal Medicine Foundation launched the



Figure 4. Summary of (A) diagnostic imaging, (B) diagnostic blood work, and (C) treatment recommendations selected by HCPs upon suspicion of inflammatory back pain. Percentages are the proportion of HCPs among those who elected to order diagnostic imaging, order diagnostic blood work, or treat the patients themselves, respectively. Abbreviations: CCP, cyclic citrullinated protein; CRP, C-reactive protein; CT, computed tomography; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; HCP, health care provider; HLA-B27, human leukocyte antigen B27; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drug; PET, positron emission tomography. [Color figure can be viewed at wileyonlinelibrary.com]

"Choosing Wisely" campaign in 2012, which included recommendations from the American College of Rheumatology and the Canadian Rheumatology Association against ANA testing if a high pretest probability exists for immune-mediated and/or active disease (12,13). Because many HCPs are still selecting ANA for initial diagnostic workup, greater awareness of these recommendations is warranted. Erythrocyte sedimentation rate and C-reactive protein were appropriately recognized as initial diagnostic tests by approximately 90% of the surveyed providers. Only 76% of HCPs would order HLA-B27 testing in patients with suspected IBP, suggesting a lack of awareness about HLA-B27 as a biomarker of AS. Among providers who would order imaging, the majority selected x-ray of the pelvis or spine as initial imaging modalities in patients with chronic back pain lasting longer than 3 months. In routine



Figure 5. Summary of (A) HCP patient referral preferences, (B) reasons that prevented patients from seeing another specialist right away, and (C) HCP ranking of referral attributes by importance. SUCRA is a summary score describing the overall ranking of a specific choice among all available choices. Values range from 0% to 100%; higher scores indicate a higher ranking of importance by HCPs. Abbreviations: HCP, healthcare provider; SUCRA, surface under the cumulative ranking. [Color figure can be viewed at wileyonlinelibrary.com]



Figure 6. Summary of HCP ranking of educational or learning materials by importance. SUCRA is a summary score describing the overall ranking of a specific choice among all available choices. Values range from 0% to 100%; higher scores indicate a higher ranking of importance by HCPs. Abbreviations: HCP, healthcare provider; SUCRA, surface under the cumulative ranking. [Color figure can be viewed at wileyonlinelibrary. com]

clinical practice, if radiographs are unremarkable or equivocal for sacroiliitis and there is ongoing clinical suspicion for AS, magnetic resonance imaging of the pelvis should then be considered (14).

Of HCPs who indicated that they prefer to treat patients with suspected IBP themselves, approximately 80% would treat them initially with NSAIDs and physical therapy consistent with current treatment recommendations for AS. However, 40% would recommend biologic therapy. Although biologics are recommended for the treatment of AS in patients with inadequate response to NSAIDs (15), the therapy is expensive and may cause serious side effects, particularly if the diagnosis is not correct. Biologic therapy should be reserved until the diagnosis of AS is confirmed by a rheumatologist. A similar proportion of HCPs (40%) would prescribe opioids, although there is no evidence supporting the efficacy of opioids for the treatment of IBP and current AS treatment guidelines recommend the use of opioids to relieve pain only in patients with an inadequate response to NSAIDs and biologics (15). Approximately one-third of HCPs would recommend disease-modifying antirheumatic drugs for IBP, which is not the standard of care in patients with AS who have back symptoms.

The majority of HCPs stated they would refer the patients to another specialist, of whom three-quarters would refer the patients to a rheumatologist. HCPs reported long waiting times and insurance restrictions as the two primary reasons preventing their patients from being able to see a specialist right away, and most reported a wait time of up to 2 months for their patients to see a specialist once a referral was made. One-third of the surveyed HCPs reported the lack of adequate specialists nearby as a reason for delayed evaluation. One-quarter of the surveyed HCPs would refer patients only if their symptoms did not improve with initial treatment, possibly delaying the diagnosis.

To our knowledge, this is the largest study of HCPs undertaken in the United States to understand reasons for delays in the referral of patients with IBP and other clinical features suggestive of AS. Nearly two-thirds of primary care HCPs reported that they were the first HCPs consulted by patients with suspected IBP, suggesting that primary care providers are often the "gatekeepers" to diagnosis and that targeted education on the signs and symptoms of AS among primary care providers may improve referral rates and yield a timely diagnosis of AS. A significantly higher number of resident physicians in primary care referred unannounced, standardized patients simulating axial and peripheral spondyloarthritis to a rheumatologist after learning about the diseases compared with controls (16). This supports the idea that further education about IBP and AS may improve referral rates.

Improved referral strategies in primary care may yield a timelier diagnosis of AS. Several studies have reported numerous referral strategies developed for primary care physicians and other specialists, with the aim of improving the referral of patients with chronic back pain and possible AS to a rheumatologist (17–24). The optimal referral strategy may differ from one health care system to another because of differences in health care infrastructures. Although IBP criteria effectively select patients in primary care for referrals to rheumatology, the specificity of IBP alone as a diagnostic utility is low in rheumatology settings (10). The use of IBP as the singular referral factor may be feasible in situations in which HLA-B27 testing and/or imaging workup are unavailable because several studies have shown that approximately onethird of patients referred to a rheumatologist because of IBP were eventually diagnosed with AS (18,24). However, this strategy is dependent on the appropriate recognition of IBP among general practitioners. Therefore, proper education and training of general practitioners may strengthen the usefulness of referral strategies to rheumatologists.

Our results should be interpreted in the context of limitations inherent to most survey studies, including selection bias and sample representativeness. Our study may be subject to potential participant/volunteer bias, which may lead to an underestimation or overestimation of results. Although a large sample of HCPs representing the spectrum of specialties who encounter patients with symptoms associated with IBP responded to the survey, study results were based on HCP self-reported answers, and no corroboration was performed with actual patient medical records. Selection bias was also a potential limitation of this study because HCPs were recruited through a panel and their feedback may be different than that of those who do not participate in a panel. Selection bias may limit generalizability to the overall HCP population in the United States. The survey was not specific enough to differentiate between patients with IBP who may have had AS versus nonradiographic axial spondyloarthritis; because nonrheumatology HCPs were more familiar with AS than with axial spondyloarthritis, "ankylosing spondylitis" was used to encompass these conditions.

In conclusion, our study broadens the understanding of the pathway for assessing, diagnosing, and referring patients with chronic back pain suggestive of IBP by various HCPs to a rheumatologist in the United States. The study indicated that most surveyed HCPs had difficulty identifying the characteristic features of back pain suggestive of IBP, such as back pain that gets better with activity, even though this parameter has the highest sensitivity for the diagnosis of AS. Additionally, HCPs selected diagnostic tests such as RF and ANA despite very low pretest probability of RA and systemic lupus erythematosus in patients with chronic back pain. Most of the patients with chronic back pain initially sought care from primary care physicians (internists and family practitioners). The study also identified specific areas in which a delay in referral of patients with chronic back pain suggestive of AS can occur, such as insurance restrictions, long wait times for rheumatology consults, and lack of close proximity to specialists. Additional education could be provided to HCPs and patients to reduce the time to diagnosis for these patients.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual contact, and all authors approved the final version to be published. Dr. Magrey had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study conception and design: Magrey, Yi, Wolin, Price, Chirila, Davenport, Park. Acquisition of data: Magrey, Yi, Wolin, Price, Chirila, Davenport, Park. Analysis and interpretation of data: Magrey, Yi, Wolin, Price, Chirila, Davenport, Park.

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