original report

Pathology Services in Nigeria: Cross-Sectional Survey Results From Three Cancer Consortia

Peter Ntiamoah, PhD, MPH[1]; Ngozi R. Monu, PhD[2]; Fatimah B. Abdulkareem, MD[3]; Kayode A. Adeniji, MBChB[4]; John O. Obafunwa, MD[5]; Akinwumi O. Komolafe, MBChB[6]; Clayton Yates, PhD[7]; Ernest Kaninjing, DrPH[8]; John D. Carpten, PhD[9]; Bodour Salhia, PhD[9]; Folake T. Odedina, PhD[10]; Marcia Edelweiss, MD[1]; T. Peter Kingham, MD[1]; and Olusegun I. Alatise, MD[6]

abstract

PURPOSE Cancer incidence is increasing in sub-Saharan Africa, yet there is little information on the capacity of pathology laboratories in this region. We aimed to assess the current state of pathology services in Nigeria to guide strategies to ensure best practices and improve the quality of surgical specimen handling.

METHODS We developed structured pathology survey to assess tissue handling, sample processing, and immunohistochemistry (IHC) capabilities. The survey was distributed electronically to 22 medical centers in Nigeria that are part of established cancer consortia. Data were collected between September and October 2017.

RESULTS Sixteen of 22 centers completed the survey in full. All 16 institutions had at least one board-certified pathologist and at least one full-time laboratory scientist/technologist. The majority of responding institutions (75%) reported processing fewer than 3,000 samples per year. For sample processing, 38% of institutions reported manual tissue processing and 75% processed biopsies and surgical specimens together. The average tissue fixation time ranged from 5 to more than 72 hours before processing and paraffin embedding. Half of the institutions reported having no quality assurance processes to evaluate hematoxylin and eosin–stained slides, and 25% reported having no written operating procedures. Half of the participating institutions have a facility for routine IHC staining, and among these there was considerable variability in processes and validation procedures. External proficiency testing was not common among surveyed sites (38%).

CONCLUSION Data from 16 Nigerian medical institutions indicate deficiencies in standardization, quality control, and IHC validation that could affect the reliability of pathology results. These findings highlight addressable gaps in pathology services that can ensure accurate diagnosis and follow-up for the growing number of patients with cancer in this region.

INTRODUCTION

Poor quality and limited access to pathologic and laboratory medicine in low- and middle-income countries (LMICs) can result in delayed and inaccurate cancer diagnoses. Pathology inadequacies can have serious consequences, including inappropriate follow-up, delayed or ineffective treatment, and poor patient outcomes. Despite its important role in guiding clinical care, pathology fails to receive the necessary investment and attention needed to perform its essential functions in LMICs.[1,2] Given the projection that approximately 80% of the global cancer burden will be in LMIC by 2030 (WHO, 2010), addressing fundamental gaps in cancer diagnosis is an essential component of a cancer control strategy in resource-limited settings.

Pathology laboratories struggle to meet the growing needs of patients with cancer in Africa.[3] In sub-Saharan Africa (SSA), most countries have underinvested in pathology services, despite having the highest age-standardized breast cancer mortality rate in the world.[1,4] Many pathology laboratories in SSA do not have the infrastructure or technologies that are available in high-income countries. The need for pathology improvement in SSA has been recognized by several groups,[5-8] who point to necessary systems, quality assurance (QA; established processes to meet quality requirements), and workforce improvements as well as the need for technical standards for tissue handling and processing and standard operating procedures (SOPs) for pathology laboratories.

International Standards Organization (ISO) 15189: 2012 is the international reference for best laboratory practices.[9] ISO 15189:2012 is not required in most countries, but it is the most common reference for quality in pathology laboratories and includes

ASSOCIATED CONTENT

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

We aimed to assess the current state of pathology services in Nigeria to guide strategies to ensure best practices and improve surgical specimen handling.

Knowledge Generated

Data from 16 cancer consortia–affiliated Nigerian medical institutions indicate deficiencies in standardization, quality control, and immunohistochemistry validation that could affect the reliability of pathology results.

Relevance

These gaps in pathology services and practices can be addressed to ensure quality specimen handling and accurate pathologic results for the growing number of cancer cases in Nigeria.

technical specifications for personnel, environmental conditions, laboratory equipment and consumables, examination processes, quality control, reporting, release of results, and information management. However, accurate data and standards pertaining to the current state of pathology services to work toward these standards are lacking in SSA. To date, studies that have assessed pathology needs in the region have focused on the total number of pathologists and the lack of necessary resources that would otherwise ensure accurate testing and reporting. These include essential infrastructure, basic equipment, skilled personnel, equipment maintenance,[5,6,10,11] training materials and services,[5,11,12] and the quality of pathology reports.[13,14] A more detailed look at current minimum standards, QA processes, use of SOPs, and sample handling procedures, with consideration of ISO standards, is warranted.

Nigeria leads the WHO African region in cancer burden, with breast, prostate, cervical, colorectal, and liver as the top cancers by incidence.[15] Clinicians depend heavily on pathologic findings to assess severity, prognosis, and potential treatments for these cancers.[1,16] Nigeria has seen an improvement in the number of pathologists per population[17,18]; however, the majority of pathology services remain rudimentary compared with high-income countries, and access to high-quality pathology services is still lacking. Here, we report the results of a survey conducted to assess the current state of surgical pathology laboratory practices from a subset of cancer consortia–affiliated institutions in Nigeria to guide future efforts to ensure best practices and improve the quality of surgical pathology specimen handling.

METHODS

Participants

A convenience sample of 22 Nigerian medical institutions that are members of either the African Research Group for Oncology, the Prostate Cancer Transatlantic Consortium, or the Nigerian Breast Cancer Consortium were selected to complete an electronic survey on pathology practices and capacity. The institutions represent a cross-section of Nigeria's health care centers. Targeted study participants were pathologists, administrators, or designated individuals with knowledge of the pathology services of their institution. Surveys were electronically distributed to participants using each consortium's listserv. Data collection took place from September to October 2017. This study occurred before a pathology training workshop held in November 2017 in Lagos, Nigeria, that focused on developing SOPs to improve pathology practice in West Africa, with a focus on Nigeria.

Survey Instrument

A 40-item, English-language, structured pathology survey instrument was developed by the investigators using expert opinions on quality pathology laboratory services and best practices for surgical specimen handling. An independent group of pathologists, histotechnologists, and administrative personnel tested the questionnaire to establish content validity. Information requested related to tissue handling and processing, immunohistochemistry (IHC), and quality control (QC; processes to fulfill quality requirements). Survey questions are provided in the Data Supplement. Qualtrics software (Qualtrics, Provo, UT) was used for survey administration and data management.

Data Analysis

Data analysis was performed using SPSS version 23.0 (SPSS, Chicago, IL). The nominal variable yes/no was used as a data point for each question. Due to the small sample size, no comparative statistical analyses were performed. Binary data are reported as number and percentage for each question.

RESULTS

Twenty-two institutions completed the survey. Information was missing in the responses from six institutions, and these were excluded from analysis, making the final response rate 73%. Characteristics of the respondent institutions are listed in Table 1. Thirteen (81%) of 16 institutions were university hospitals, two (13%) were private or independent hospitals, and one (6%) was a proprietary hospital. Approximately 94% of responding

TABLE 1. Characteristics of Participating Institutions

Characteristic	No. of Institutions (N = 16; %)
Fully functional anatomic pathology laboratory to handle pathology needs	
Yes	15 (94)
No	1 (6)
No. of board-certified pathologists	
1-4	10 (63)
≥ 5	6 (37)
No. of anatomic pathology (physician) trainees	
1-3	3 (19)
≥ 4	11 (69)
Unknown	2 (12)
No. of full-time laboratory scientists/technologists	
1-6	10 (63)
7-12	6 (37)
Anatomic pathology services offered	
Surgical pathology only	1 (6)
Surgical pathology and autopsy	7 (43)
Surgical pathology, autopsy, and immunohistochemistry	4 (25)
Surgical pathology, autopsy, intraoperative frozen section, and immunohistochemistry	2 (13)
Surgical pathology, autopsy, immunohistochemistry, brightfield in situ hybridization, and tissue-based polymerase chain reaction	2 (13)
Average annual volume of cases and tissue blocks prepared	
≤ 1,000	5 (31)
1,001-2,000	2 (13)
2,001-3,000	5 (31)
≥ 3,001	3 (19)
Unknown	1 (6)

institutions reported having a fully functional pathology laboratory that consistently handles routine anatomic pathology requests. All institutions indicated that they have at least one board-certified pathologist and at least one full-time laboratory scientist/technologist; 69% have a minimum of four pathology residents.

Pathology services at the 16 sites included analysis of biopsies and surgical specimens from multiple organ sites, with variations across institutions (Table 1). Three fourths of institutions reported annual specimen volume of fewer than 3,000, whereas three institutions (19%) reported handling more than 3,000 samples per year. More than 3,000 surgical accessions per year is considered high volume in Nigeria.[17] Although our questionnaire did not discriminate between biopsies and resections, pathologists in high-volume tertiary centers would likely handle a complex patient mix.[19,20]

We also assessed the standard tissue processing procedures at the institutions (Table 2). Approximately 88% of respondents fix tissues in 10% neutral buffered formalin. Whereas 38% of institutions reported manual tissue processing, others used an automated tissue processor, such as those from Leica Biosystems (Wetzlar, Germany) or Thermo Fisher Scientific (Waltham, MA). In terms of processing, 75% of institutions process biopsies and surgical specimens together, whereas 25% process them separately. All centers use xylene as a clearing agent, and 56% use ethanol for dehydration.

Reported average tissue fixation time at the centers ranged from 5 hours to more than 72 hours (Table 2). For biopsies, 81% of institutions reported formalin fixation of 6 to 72 hours, 6% fix tissues for less than 6 hours, and 13% fix tissues for more than 72 hours. Half of the institutions fix surgical specimens for 6 to 72 hours, and 50% fix tissues for more than 72 hours.

Three fourths of institutions have written SOPs for tissue processing, whereas others (25%) reported no SOP manual. Half of the institutions reported the use of a QA process to evaluate hematoxylin and eosin (H&E) –stained slides on a daily basis. Of these eight institutions, 88% report that H&E QC evaluations are performed by both laboratory scientists and pathologists. One institution reported the use of a QA process but could not indicate whether it was performed by laboratory scientists or pathologists (Table 2).

The survey also assessed IHC services and techniques (Table 3). Approximately 47% of respondents send their IHC to reference laboratories, and eight institutions reported having a facility for routine IHC staining. Of the intuitions performing IHC on-site, three fourths cut IHC sections at 3 to 5 μm; one center (13%) reported requiring 2-μm sections for IHC staining. Most institutions (63%) use low-pH antigen retrieval solutions, and retrieval time varied between 15 minutes and more than 60 minutes (Table 3). Approximately 88% of institutions perform IHC manually; one institution (13%) reported the use of a Ventana autostainer (Ventana Medical Systems, Oro Valley, AZ). All institutions reported using heat-induced epitope retrieval solutions to unmask antigen binding sites. The majority of institutions (75%) perform antigen retrieval using either a steamer (25%), pressure cooker (25%), water bath (25%), or microwave oven (13%). All laboratories reported the use of 3,3′-diaminobenzidine chromogen for IHC staining.

The expected turnaround time for IHC requests varied across institutions from 25 to 48 hours to more than 72 hours. Although 63% of respondents performing IHC on-site have written procedures to validate predictive IHC makers, none of these institutions tests a minimum of 20 cases for validation of nonpredictive markers. It is important to include a sufficient number of patients in validation

TABLE 2. Tissue Processing and Hematoxylin and Eosin Staining

Variable	No. of Institutions (N = 16, unless otherwise noted; %)
Use of quality assurance process for evaluating hematoxylin and eosin stains daily	
Yes	8 (50)
Performed by (N = 8)	
Pathologists	0
Laboratory scientists	0
Both	7 (88)
Unknown	1 (12)
No	8 (50)
Type of fixative for specimen processing	
10% neutral buffered formalin	14 (88)
Commercial formalin alternative	2 (12)
Laboratory method for processing specimens	
Manually	6 (37)
Automated tissue processor	10 (63)
Type of processor (N = 10)	
Shandon	4 (40)
Leica	5 (50)
Unknown	1 (10)
Available written standard operation manual for tissue processing	
Yes	12 (75)
No	4 (25)
Separation of small size specimens (biopsies) from larger tissue samples for processing	
Yes	4 (25)
No	12 (75)
Average length of fixation for biopsies, hours	
5	1 (6)
6-72	13 (81)
> 72	2 (13)
Average length of fixation for larger tissue samples, hours	
5	0
6-72	8 (50)
> 72	8 (50)
Dehydration reagent	
Alcohol blend	0
Ethanol	9 (56)
Isopropanol	2 (13)
Reagent alcohol	5 (31)
Clearing reagent	
Xylene	16 (100)
Decalcification reagent	
EDTA and formic acid	2 (13)
Formic acid only	9 (56)
Hydrochloric acid only	3 (18)
Formic acid and hydrochloric acid	2 (13)

studies for proper characterization of the antibody, performance parameters, and interpretation criteria.[21,22] Approximately 75% of the laboratories do not perform IHC on cytologic specimens, and 75% do not include decalcified specimens in the validation. Final IHC protocol approval—ie, antigen retrieval, antibody dilution, and incubation time—at 75% of the institutions is made by laboratory scientists/managers, not pathologists. Only 38% of the institutions reported external proficiency testing, a quality assessment tool that aids in evaluating current knowledge, standardizing processes, and identifying areas for improvement. Most institutions (75%) have a process to investigate cases that did not meet the expected turnaround time.

DISCUSSION

The need for oncology services in SSA has increased in recent years, and the demand is projected to continue to rise in the foreseeable future.[23,24] Pathology laboratories in the region provide a critical service that guides both clinical decision making and cancer research initiatives. Accurate diagnosis and high-quality tissue preservation are important for immediate and long-term patient outcomes. Reliability and validity of pathology laboratory processes are paramount. Our survey assessed pathology capacity and practices in cancer consortia–affiliated institutions in Nigeria and identified several areas for improvement in pathology laboratory practices, including variability/inadequacies in tissue handling and processing, standardization, QC processes, and IHC procedures and validation.

Many prior studies report a shortage of pathologists in SSA,[2,25,26] an observation consistent with our survey findings—63% of the institutions reported four or fewer certified pathologists. A 2011 to 2013 survey that assessed pathology capacity in SSA found that pathologists per population ranged from 84,133 persons per pathologist in Mauritius to 9,264,500 persons per pathologist in Niger[26] compared with 5.7 pathologists per 100,000 persons in the United States.[27] In addition to clinical responsibilities—that

TABLE 3. Immunohistochemistry Services and Techniques

Variable	Institutions With IHC Staining Facility (N = 8; No., %)	Institutions Without IHC Staining Facility (N = 8; No., %)
Frequency of IHC staining		
Daily	2 (25)	
Weekly	3 (37)	
Biweekly	1 (13)	
When needed	2 (25)	
How IHC needs are handled		
Block sent to an outside laboratory for specific antibodies, without interpretation		1 (13)
Block sent to an outside laboratory for specific antibodies, with interpretation		7 (87)
Availability of antibody validation process of reference laboratory		
Yes		0
No		8 (100)
Specific tissue/block submission requirements by reference laboratory		
Yes		3 (37)
No		4 (50)
Not sure		1 (13)
Method of IHC staining		
Automated staining	1 (13)	
Manual staining	7 (87)	
Antigen retrieval method		
Protease digestion	0	
HIER, steamer	2 (25)	
HIER, microwave	1 (13)	
HIER, pressure cooker	2 (25)	
HIER, water bath	2 (25)	
HIER, automated stainer	1 (13)	
Buffer type (HIER usage)		
Low pH	5 (62)	
High pH	2 (25)	
Unknown	1 (13)	
Total retrieval time (HIER usage), minutes		
> 15 to < 30	2 (25)	
> 30 to < 45	2 (25)	
> 45 to < 60	2 (25)	
> 60	1 (13)	
Unknown	1 (13)	

(Continued on following page)

is, providing laboratory services oversight and issuing pathology reports—almost all pathologists report also training pathology residents. The increased demand on pathologists' time, coupled with growing caseloads and fewer support staff, can affect the turnaround time and oversight of laboratory services.[26] In our study, approximately 60% of responding institutions reported a turnaround time for IHC of 3 days or more, and 40% of sites reported no QA program to evaluate H&E stains on a daily basis. The extended turnaround time and insufficient QA oversight may result from skilled staff who are overwhelmed with clinical specimens, similar to observations of laboratory services in Ethiopia.[28]

Without adequate QC processes, laboratory staff may not identify nonconformance events and address them promptly. Moreover, more than 60% of institutions surveyed reported no external proficiency testing. This finding is consistent with prior observations that indicate that more than 75% of SSA countries had pathology laboratories that failed to meet internationally recognized QA standards.[29] External proficiency testing ensures that laboratory practices conform to required quality standards needed for patient care. Lack of external quality assessment not only impedes the identification of discrepant laboratory processes and systemic errors, but may also affect the quality of patient results and ultimately patient management.

The process of producing formalin-fixed, paraffin-embedded tissue blocks and sections requires the standardization of all preanalytical and analytical processing stages by individual laboratories. Wide interlaboratory variation in sample handling, processing, and/or methodology may adversely affect the reliability of downstream assay results and tissue quality for future research use. Our study demonstrates that 75% of surveyed institutions process biopsies and surgical specimens together, a practice that can result in either overprocessing of small samples or underprocessing of larger surgical specimens.[30] Such suboptimal processing can affect tissue morphology, quality of stains, and ancillary testing, and ultimately lead to delays in reporting and/or diagnostic errors.[31-33] In addition, approximately 40% of laboratories in our study reported processing samples manually. Routine manual tissue processing can introduce variation and is less consistent and reproducible than automated methods.[34] Manual tissue processing also requires close monitoring of factors, such as reagent quality, temperature, solution pH, and time. Finally, 50% of sites reported having no QA process to assess the quality of basic H&E stains, a type of stain that is easily influenced by the nature of tissue handling and processing.[35,36] Widespread manual tissue handling and processing, processing of biopsy and surgical samples together, and insufficient reagent QC all represent significant sources of variability that could critically affect formalin-fixed, paraffin-embedded tissue block quality.

Most pathology laboratories in SSA operate from 9 AM to 5 PM, yet 81% of respondents reported fixation and

TABLE 3. Immunohistochemistry Services and Techniques (Continued)

Variable	Institutions With IHC Staining Facility (N = 8; No., %)	Institutions Without IHC Staining Facility (N = 8; No., %)
Cut thickness, μm		
2	1 (13)	
3-5	6 (75)	
Unknown	1 (13)	
Detection reagent		
HRP polymer kit with DAB	8 (100)	
Available written procedures to validate predictive and nonpredictive antibodies		
Yes, for predictive markers only	5 (63)	
Unknown	3 (37)	
Include a minimum of 20 cases in nonpredictive antibody validation		
Yes	0 (0)	
No	8 (100)	
Include cytology specimens in antibody validation		
Yes	1 (13)	
No	1 (13)	
Do not perform IHC on cytology specimens	6 (74)	
Include decalcified specimens in antibody validation		
Yes	1 (13)	
No	5 (62)	
Do not perform IHC on decalcified specimens	2 (25)	
Expected turnaround time, hours		
< 24	0 (0)	—
25-48	3 (38)	—
49-72	2 (24)	—
> 72	3 (38)	8 (100)

Abbreviations: DAB, 3,3′-diaminobenzidine; HIER, heat-induced epitope retrieval; HRP, horseradish peroxidase; IHC, immunohistochemistry.

processing times of 6 to 72 hours. Thus, the total tissue processing time may extend beyond laboratories' normal time of operation, and manual processes may therefore go unmonitored or be segmented over several days. Longer manual tissue processing time and inadequate control of reagent quality, time in specific reagents, and temperature can affect tissues quality and may permanently damage protein and nucleic acid targets of subsequent IHC and molecular testing, respectively.[37,38] Based on the College of American Pathologists/American Society of Clinical Oncology guidelines for reliable IHC stains in breast specimens,[39,40] which specify 6 to 72 hours for fixation time, 20% and 10% of the surveyed sites underfix or overfix biopsy samples, respectively; 40% overfix resection samples.

One fourth of responding institutions reported having no written SOPs. It is recommended that pathology laboratories have written SOPs that delineate step-by-step procedural instructions, troubleshooting, and QC aspects for each process.[6,41] SOPs outline a laboratory's policies, processes, and infrastructure and provide the framework for any accrediting agency evaluating local practices against expected laboratory standards.[42,43] A written SOP manual is essential for adequate training of all technical staff, maintaining quality, reducing variability of laboratory processes, and ensuring sufficient clinical oversight of laboratory activities.[42] Establishing SOPs in these settings may improve workflow efficiency and minimize errors and variability in laboratory processes.[44]

IHC provides diagnostic confirmation and it is important to control parameters that could affect protein preservation to minimize false-negative staining. Accurate IHC results rely largely on slide preparation techniques—that is, tissue fixation, processing, antigen retrieval, primary antibody incubation, reagent pH, and environmental factors—and interpretation of the staining pattern.[45] Antigen retrieval time, for instance, depends on fixation type and length, detection system sensitivity, retrieval solution pH or enzyme concentration, and intended antibody target.[46,47] Our study found a number of gaps in technical and QC measures that would ensure the standardization, reproducibility, accuracy, and validity of IHC results. The majority of the surveyed laboratories with IHC capabilities perform tests manually using a variety of appliances (steamer, microwave, pressure cooker, and water bath) for heat-induced epitope retrieval. Some of these appliances are not ideal. Microwaves tend to produce uneven heat distribution and steamers or pressure cookers may cause temperature variations and tissue disruption.[48,49] Approximately one third of laboratories perform IHC on 2- to 3-μm sections, even though the recommended thickness is 4 to 5 μm; inappropriate section thickness can negatively affect the proportion of positive and negative cells and ultimately affect diagnostic accuracy.[50]

More than 40% of surveyed laboratories have no written procedures for basic antibody validation. Lack of validation procedures accompanied by suboptimal section thickness could affect staining quality and the interpretation of results. We also found that the final antibody working protocol—that is, retrieval and incubation time, antibody dilution, and staining intensity—at most sites is determined by a nonpathologist. Only 25% of participating laboratories reported final approval by a pathologist or a designee. IHC staining interpretation requires the integration of multiple parameters,

including demographic information, tumor location, potential tumor biology, the antigen's expression in normal versus neoplastic tissues, and pertinent clinical history. Although there are no known criteria with which to assess the competency of nonpathologist staff for IHC protocol approval, integration of pertinent clinical information may not be well understood by nonpathologists. Approval of IHC working protocols by nonpathologists may indicate insufficient clinical oversight of laboratory services.

Limitations of the current study include the cross-sectional nature and small sample size obtained by convenience sampling. Caution must be exercised in generalizing the findings. Most of the participating centers are in the southwest part of Nigeria, and the findings may not reflect the conditions in the entire country. Tissue size and types were not captured in the survey; thus, a correlation between tissue size/type and fixation time could not be established to aid in the interpretation of the fixation issues identified. There was a high representation of tertiary hospitals, likely because of the higher likelihood of such institutions to offer pathology services in LMICs.[1] In addition, the analysis is based on information reported by surveyed sites and its accuracy might have been influenced by response bias. However, the current study demonstrates the feasibility and value of a pathology survey in this region. A larger-scale survey that addresses additional pathologically relevant areas is warranted to further evaluate gaps in pathology laboratories' readiness to respond to current and future conditions in SSA.

A strength of this study is the identification of gaps in pathology services that would be inexpensive to address. On the basis of our findings, we recommend the creation of internal standards and guidelines to ensure high-quality pathology practices. Transitioning to the use of tissue processors over manual tissue processing would improve consistency. In the absence of financial resources for such a transition, establishing SOPs and providing relevant training in manual tissue processing, guided by pathologists, is critical. Furthermore, we recommend routine external quality assessment—proficiency testing—to validate that processes are correctly followed and technical and diagnostic standards are routinely achieved. Ultimately, these steps are essential for ensuring best histopathologic practices to support quality cancer care in Nigeria and guide quality improvement efforts, such as enrollment in the WHO Stepwise Laboratory (Quality) Improvement Process Toward Accreditation (SLIPTA) program.

In conclusion, key themes highlighted in the current study are the inadequate standardization of protocols and processes within the preanalytical, analytical, and postanalytical phases of pathologic analysis. There is also evidence of a lack of adherence to guidelines across institutions in the region with a potential impact on quality, reliability, and pathology results. These are addressable gaps in pathology services that can ensure accurate diagnosis and quality specimen handling in Nigeria.

AFFILIATIONS

[1]Memorial Sloan Kettering Cancer Center, New York, NY
[2]Weill Cornell Medical College, New York, NY
[3]University of Lagos, Lagos, Nigeria
[4]University of Ilorin Teaching Hospital, Ilorin, Nigeria
[5]Lagos State University Teaching Hospital, Lagos, Nigeria
[6]Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria
[7]Tuskegee University, Tuskegee, AL
[8]Georgia College and State University, Milledgeville, GA
[9]University of Southern California, Los Angeles, CA
[10]University of Florida Lake Nona Research and Academic Center, Orlando, FL

CORRESPONDING AUTHOR

Olusegun I. Alatise, MBChB, MSc, Obafemi Awolowo University Teaching Hospitals Complex, PMB 5538, Ile-Ife, Osun, Nigeria; e-mail: segunalatishe@gmail.com.

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AUTHOR CONTRIBUTIONS

Conception and design: Peter Ntiamoah, Kayode A. Adeniji, John D. Carpten, Folake T. Odedina, T. Peter Kingham, Olusegun I. Alatise

Financial support: Kayode A. Adeniji

Administrative support: Folake T. Odedina

Provision of study materials or patients: Fatimah B. Abdulkareem, Kayode A. Adeniji, Folake T. Odedina

Collection and assembly of data: Peter Ntiamoah, Ngozi R. Monu, Kayode A. Adeniji, John O. Obafunwa, Folake T. Odedina, Olusegun I. Alatise

Data analysis and interpretation: Peter Ntiamoah, Ngozi R. Monu, Fatimah B. Abdulkareem, Akinwumi O. Komolafe, Clayton Yates, Ernest Kaninjing, Bodour Salhia, Folake T. Odedina, Marcia Edelweiss, T. Peter Kingham, Olusegun I. Alatise

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Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Clayton Yates

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John D. Carpten
Consulting or Advisory Role: Ashion Analytics
Patents, Royalties, Other Intellectual Property: Methods related to precision medicine know-how

T. Peter Kingham
Consulting or Advisory Role: Physician Education Resource

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