Message from the President
Herbert Chen, MD

I am absolutely honored and thrilled to be your President. I want to congratulate our new AAES Secretary James Lee. I know he will do a fantastic job and I look forward to working with him this year. I also want to congratulate our new Vice President Sonia Sugg, Councilor Jen Rosen, Councilor John Lew, and President-Elect Allan Siperstein. We could not be more fortunate to have such a talented leadership team, along with our Treasurer Sareh Parengi and Recorder Paul Gauger.

I want to update you on a few ongoing and new initiatives that we will be focusing on through our current committees and new task forces. We had more than 80 AAES members self-nominate for these positions, and I am happy to announce that I was able to appoint EVERYONE to a position. Thank you so much for your dedication to the AAES! In order to help the AAES better serve our members, I have convened four new Task Forces to address critical issues facing the AAES and our membership:

Patient Advocacy Task Force: Co-Chairs Kepal Patel and Sally Carty. This group will focus on how we can optimize our collaboration with patient advocacy groups such as the ParaTroupers, ThyCa, and Graves' Disease and Thyroid Foundation.

Endocrine Surgery Identity Task Force: Co-Chairs Jennifer Kuo and Allan Siperstein. This group will develop outreach and marketing strategies to inform health policy leaders, health care providers, patients, and the public about the contributions and expertise of Endocrine Surgeons.

Career Development Task Force: Co-Chairs Tracy Wang, Fiuwu Nwariaku and John Lew. This group will identify opportunities to promote Endocrine Surgeons as leaders in American Surgery. Part of their mission will be to develop strategies to increase the number of endocrine surgery programs nationally.

Mission Birmingham Task Force: Building upon the success of the Calgary Project that created the AAES Patient Education website, this group will update this educational content and create a new venue for patients to contribute insights into endocrine diseases in conjunction with the IT committee and the Patient Advocacy Task Force.

In addition to these new Task Forces, over the next year we will focus on a major initiative- fund raising. Treasurer Sareh Parengi will update you on our efforts throughout the year. Please, please, please consider supporting the AAES through your pledges! We need you! Donate here.

As always, our national meeting will be the highlight of the year. This year, Rachel Kelz (Program Chair) and Carrie Lubitz (Program Vice-Chair) will work closely with...
and click on Dues Renewal or contact Margaret Cloyd in Member Services by clicking here.

SAVE THE DATE

2019
Los Angeles, CA
April 7-9, 2019
Local Arrangements Chair: Michael Yeh, MD
Program Chair: Rachel Kelz, MD
Program Vice-Chair: Carrie Lubitz, MD

2020
Birmingham, AL
Dates TBD
Local Arrangements Chair: John Porterfield, MD

2021
Cleveland, OH
Dates TBD
Local Arrangements Chair: Vikram Krishnamurthy, MD

MEETINGS OF INTEREST

AACE/ACE Advanced Neck Ultrasound Training Course
September 8-9, 2018
Orlando, FL

88th Annual Meeting of the American Thyroid Association
October 3-7, 2018
Washington, DC

ACS Clinical Congress
October 21-25, 2018
Boston, MA

DONATE TO THE AAES FOUNDATION

Message from the Secretary
Rebecca S. Sippel, MD

Greetings from the Secretary office of the AAES! My three years as Secretary of the AAES has come to an end. While the years have gone by quickly, it is amazing to look back and see the changes that have happened in just the past few years. We ended our relationship with BSC management and ran a comprehensive management company search and have now completed our second year with AMR management, based in Lexington, KY. Under the direction of AMR, we established a strategic plan for our organization and completed two strategic planning sessions to help us keep on track with our plan. We launched a new website, with a members only portal and comprehensive directory. We also established a social media presence on both Facebook and Twitter. We have made the organization more inclusive by opening up all committee positions for self-nomination and created a new officer position (Treasurer) and two new standing committees. We have streamlined the membership application process to allow our fellows to transition to an active member more easily and quicker and worked to provide opportunities for them to serve the organization. The management of CESQIP was transitioned outside of the AAES to a separate 501c3 overseen by the ESQ Foundation and it continues to grow and flourish with the guidance of Arbometrix and the leadership of Dr. Barry Inabinet. We have run 3 highly successful meetings and have incorporated some exciting changes including a co-located meeting with the Endocrine Society last year and this year a new Advanced Endocrine Surgery CME course as well as some industry sponsored symposiums which have really help to offset the costs of running our annual meeting and allowed us to provide lunches as part of the program.

This year we again offered up a self-nomination process for committee positions within the AAES. We were overwhelmed with the response, but are thrilled to see the excitement of our members and their desire to serve the organization. Dr. Chen has worked hard to provide opportunities for everyone that was interested in getting involved. The list of the newly appointed committee members can be found here: https://www.endocrinesurgery.org/About-Us/Governance/Committees.

At our last executive council meeting, we voted to upgrade the platform for the Patient Education Website and are also going to develop a more robust platform for the members only section of our website. Both of these changes will provide great opportunities to engage our membership and to improve the value of membership in our organization. These will be great additions to our organization and will give Dr. Lee an exciting task to oversee in his new role as Secretary! As part of our strategic plan we also updated the descriptions for all leadership positions within the organization and developed a reporting structure for our growing leadership structure to ensure that all committees have a direct connection to the officers of the organization. The proposed reporting structure will be piloted this year. It has been a true pleasure serving the organization over the past 3 years and I look forward to the seeing the AAES move forward with our strategic plan and to incorporate some of the amazing ideas from our membership to become an even better organization! I am thrilled to hand off the reigns to Dr. James Lee, who will do a fabulous job as Secretary of the AAES!
Message from the Vice President
Carmen C. Solorzano, MD

It was a privilege to serve as your Vice President this past year. We had 62 interesting case abstracts submitted for 2018 with eight finalists selected with the expert help of Drs. Fraker, Siperstein, Snyder and myself. By all accounts, the "interesting cases" session was a success. We had a full house and a very interactive audience. Our panel of experts Drs. Duh, Evans and Pasieka was outstanding and helped make the session very educational and fun. Congratulations to Dr. Susan Wcislo from University of Tennessee Health Science Center Memphis for winning best interesting case: Multifocal Pheochromocytoma/Paraganglioma in a 29-year-old female: surely is hereditary.

Office of the Recorder
Paul Gauger, MD

It has been a tremendous honor to serve the AAES as your Recorder over the past year. I'd like to thank Dr. Cord Sturgeon for preparing the January 2018 Issue of SURGERY during the transition of the Recorder role. Our working relationship with the SURGERY Editors and the publisher, Elsevier, remains excellent. We are grateful that the journal continues to be supportive of a dedicated full issue to serve as the proceedings of our annual meeting.

We enjoyed an outstanding scientific program at the annual meeting in Durham which was expertly designed by Dr. Wen Shen and the Program Committee. The lively discussions typical of our association were enhanced by the engagement of 14 moderators representing an inclusive cross-section of surgeons and institutions.

I'm very grateful to the 100 experts who served as reviewers for 34 submitted podium manuscripts. We expanded the reviewer pool to further reflect the diverse expertise in our association. All initial submissions received at least 3 reviews and turnaround was excellent with a median time from initial submission to final SURGERY acceptance of only 65 days. Our next annual AAES issue of SURGERY will be in January 2019 and will include all accepted podium presentation manuscripts accompanied by the full transcriptions of the discussions from the meeting. Before that, the articles will be available in e-pub format as soon as they are in production. President Herb Chen has invited editorials for four outstanding manuscripts and Dr. Zeiger's inspiring Presidential Address will also be included in the issue.

We have better aligned the function of the Recorder with the Chair of the AAES Information Technology Committee. In this role, Dr. Barbra Miller has done an outstanding job of promoting the academic work of our members using Twitter and other platforms. This recently had the benefit of generating social media conversations around abstracts during the meeting. Similarly, a single AAES article each day of January will be promoted via Twitter with a link to the full manuscript via the Elsevier portal. To improve this process, we plan to offer authors the opportunity to create high-quality visual abstracts to help promote their work in the January issue. We will assist authors with necessary guidance and feedback during the process.

Additionally, SURGERY still offers a free service called AudioSlides to authors. These are brief, webcast-style presentations that are shown next to published articles on ScienceDirect and can be viewed for free. Authors can easily modify their AAES PowerPoint presentation to create AudioSlides to provide the opportunity to explain their research in their own words in a format shareable in social media. For more information and examples, please visit http://www.elsevier.com/audioslides. Although currently being improved by Elsevier, this should be fully functional in time to promote your work in the January 2019 issue.
Thank you for all of your great contributions to science for the benefit of our patients and the AAES!

Fellowship Committee Chair Report
Melanie Lyden, MD

On August 1, 2018 we will be welcoming 24 fellows into 22 AAES accredited programs. Congratulations to the fellows and programs for a very successful match.

The Fellowship Committee had a productive year. Dr. Brian Saunders led a task force that developed guiding standards for successful completion of the AAES Comprehensive Endocrine Surgery Fellowship. These standards will be posted on the AAES website. A proposal for an ABMS Certificate of focused expertise in Comprehensive Endocrine Surgery was approved by the Executive council in May 2018. Dr. Christopher McHenry will be presenting the proposal to the ABS at their June, 2018 retreat. Dr. Thurston Drake will be championing a survey of our graduates and program directors to assess the fellowship application process. We hope to identify opportunities to improve the process. Thank you in advance for your participation.

The Fellowship Committee has been greatly appreciative of the organized and effective leadership of Dr. Tracy Wang, who transitioned as Chair in May, 2018.

Important Dates
Monday, February 26, 2018: Online application site opened.
Friday, April 27, 2018: Online application site closed.
Monday, July 23, 2018: Online ranking site opens at 9:00 AM CDT.
Wednesday, August 8, 2018: Applicant and Program rank lists due by 11:59 PM PDT.
Monday, August 13, 2018: Unmatched programs and candidates will be notified.
Thursday, August 16, 2018: Secondary rank of any unmatched programs and applicants.
Friday, August 17, 2018: Match results announced.

Additional match information can be found at www.endocrinesurgery.org, emailing the AAES Headquarters Office (match@endocrinesurgery.org) or emailing Melanie Lyden (lyden.melanie@mayo.edu).

Information & Technology Committee Chair Report
Barbra S. Miller, MD

The IT Committee continues to work hard for AAES members. New on the website (www.endocrinesurgery.org) are updated ‘Practice Guidelines’ relevant to endocrine surgeons. Find these under the ‘Resources’ tab. Follow @TheAAES on Twitter and the AAES Facebook page and look for our weekly Saturday post of newly published articles relevant to endocrine surgery. This list is also published on our website under the ‘Resources’ tab in ‘Articles of Interest’. New statements ‘Data Use Policy’ and ‘Social Media Guide to Good Use’ have been published and are available for review under the ‘About Us’ tab in the ‘Policies’ section. While in Durham at the annual meeting, the Council approved moving ahead with purchase of a learning management system to serve both our members and our patients. Please be ready and willing to help when we ask for content development on both fronts. Calgary Project 2.0 here we come! This is a great opportunity for all AAES members to get involved.

The IT committee looks forward to continuing to serve our fellow AAES members. Please contact any of the IT committee members with suggestions or concerns. Find us under the ‘About Us’ tab in the ‘Governance’ section.
Membership Committee Chair Report
James Lee, MD

Our society continues to grow and evolve. This year we added 71 new Active/Allied/Corresponding/Resident/Fellow members. AMR, our management company, has done a wonderful job streamlining the website and application process. Thank you to everyone who helped support the applications of our new members with letters of recommendation and mentorship. Special thanks to everyone who participated in the Member Value Survey from earlier in the year. Our leadership is using that feedback to help create new offerings and better serve our members. It is the engagement, dedication, and collegiality of our members that makes the AAES such a vibrant society. Please continue to spread the word about the AAES and the benefits of membership to your interested colleagues. Requirements for membership can be found online at www.endocrinesurgery.org.

Research Committee Chair Report
Kepal N. Patel, MD, FACS

The Research Committee would like to congratulate all the applicants for the Paul LoGerfo Awards and the ThyCa: Thyroid Cancer Survivors' Association Award for Thyroid Cancer Research. The competition was fierce once again and the winners of the 2018 awards were announced at the annual banquet. The two Paul LoGerfo Award winners were, Dr. Heather Wachtel, from the University of Pennsylvania, for her study, "Circulating miRNA signatures in primary hyperparathyroidism" and Dr. David Schneider, from the University of Wisconsin, for his study, "Using patient language for measuring quality of life in thyroid cancer". The ThyCa: Thyroid Cancer Survivors' Association Award for Thyroid Cancer Research winner was Dr. Lawrence Shirley, from Ohio State University Wexner Medical Center, for his study, "Integrin linked kinase facilitates communication between cancer associated fibroblasts and immune cells in papillary thyroid cancer". We look forward to their research presentations at the 2019 AAES Meeting in Los Angeles, CA.

Endocrine Surgery Reviews (ESR) is a periodic review of provocative or enlightening contemporary publications in the field of endocrine surgery. ESR is published twice a year with the newsletter. If you think a particular article deserves review in ESR, please contact the Editors-in-Chief, Drs. Nasir Nilubol (nasir.nilubol@nih.gov) and Insoo Suh (insoo.suh@ucsf.edu). Please read the most recent reviews in the ESR section of this newsletter.

Kepal Patel, MD

Education Committee Chair Report
Roy Phitayakorn, MD

The Education Committee completed its first year as a new committee and has been very busy evaluating the AAES patient education modules and developing new patient education resources. The Education Committee also vetted several new learning management systems and is proud to endorse the COACH platform. We look forward to working with the Fellowship and IT committees to develop innovative GME and CME level educational resources and products. Please do not hesitate to contact us with any further suggestions for possible projects.
Fellowship Accreditation Committee Update
Brian Saunders, MD

The fellowship accreditation committee had a successful year, with efforts to advance the association's fellowship training programs and to advance the strategic aims of the society. Congratulations to the six fellowship programs who successfully navigated reaccreditation for a full three-year cycle. Thank you, too, to the program directors and program coordinators who submitted annual program data for review. The online submission portal offered some advantages, but leaves some room for continued improvement. We have collaborated with the fellowship committee to design a fellow case experience log to better track the operative experience of our fellows. The accreditation committee also approved the guiding standards for successful completion of an AAES-accredited fellowship program in Comprehensive Endocrine Surgery to provide clear expectations for fellow candidates and programs. These standards will comprise part of the tracked outcomes reportable each year to the fellowship accreditation committee, and will serve as a cornerstone of the triennial reaccreditation process for fellowship programs.

CESQIP Update
William B. Inabnet, III, MD

CESQIP has grown to include 56 participating sites, more than 200 surgeons and greater than 28,000 case entries. The collaborative is pleased to welcome the following domestic sites: Robert Wood Johnson University Hospital, Wellspan York Hospital, Banner University Medical Center and Stanford Hospital. International sites have also commenced joining CESQIP: Chiang Rai Prachanukroh Hospital (Thailand), Seoul National University Hospital (South Korea) and Hospital Nossa Senhora de Conceição (Brazil); 12 additional sites from 5 countries in Latin America are poised to launch LA CESQIP. Please visit our new online map (https://cesqip.org/participating-sites/). A risk adjustment feature has been introduced to the outcome dashboard and a sophisticated, automated push report will be rolled out this summer to allow surgeons and programs to monitor their outcomes. To date, 14 aggregate data research proposals have been approved leading to several podium presentations and peer-reviewed publications (https://data.cesqip.org/). Finally, the time has come for me to step down as CESQIP Chair to focus on running the Endocrine Surgery Quality Foundation, the entity that oversees the finances and global strategy of CESQIP. Please join me in congratulating David Schneider and Jennifer Rosen on their appointment as the new Chair and Vice-Chair of the CESQIP Committee. To learn more about CESQIP or to enroll, please visit http://cesqip.org.

Community Based Surgeons Committee Update
Michael Starks, MD
I hope each of you was able to attend the annual meeting at the Washington Duke in Raleigh/Durham last month. It was a great meeting, a chance to reconnect and make new connections. Several of the major accomplishments of the The Community Based Surgeons committee were prominent parts of the program. The Business of Surgery panel session was organized by the committee and addressed coding and billing in endocrine surgery. Kim Vanderveen and I co-moderated the session. Speakers were Tom Connally, Kim Vanderveen, Denise Carneiro-Pila, and Allan Siperstein. The session was well attended and generated significant discussion which went through the break after it, as well as follow up online conversation. It was clear to us that many have need of a better understanding of coding and billing, regardless of institutional affiliation.

The Advanced Endocrine Surgery course was a first-time event, hopefully the first of many. It was organized by Shaghayegh Aliabadi and Erin Felger. Course moderators were Drs. Siperstein, Rosen, Kepal and Elaraj, with additional panelist who were endocrinologists, endocrine surgeons, head and neck surgeons, and surgical oncologists. All faculty donated their time, so their participation was greatly appreciated. It was built around case-based educational sessions. The course had forty attendees, including those from private practice, university and international setting. Many had not attended an AAES meeting or had not done so in a number of years. Feedback from the course was great, with all attendees reporting that it was a very valuable experience. Additionally, it provided 5.5 CME for attendees. Great job Shaghayegh and Erin!

Later this month, I will be attending a strategic planning committee meeting in Birmingham, Alabama with the rest of the AAES Council. Goals for this year will be developed during this meeting. I would greatly appreciate feedback from you to help generate these goals and tasks to accomplish them, whether you are in academic, hospital-based or private practice. One major focus of our committee is to help those practicing endocrine surgery do it better. This can be by improving educational opportunities, helping to connect us, or teach new skills. We have discussed further business of surgery panel sessions, developing endocrine surgery specific RVU benchmarking, developing endocrine surgery specific educational and patient information materials, among others. If you have suggestions for where to direct the committee’s efforts, please contact me at mstarksmd@yahoo.com. I would love to hear from you. Your comments will help better our society.

**AAES Foundation Report**

Geoffrey B. Thompson, MD

The AAES Foundation continues towards its goal of $1 million. To date, we have $562,000 in total assets, with an additional $42,000 in pledges outstanding for the Norman Thompson Fellowship. To date, $258,000 has been collected for the Norman Thompson Fellow pledges.

This year, the AAES Foundation supported Endocrine Surgery University at the $5,000 level. In addition, two awards for the best papers and best posters were provided under the Paul LoGerfo fund. An additional $2,000 was utilized for the Orlo Clark Lecture honorarium.

The AAES Foundation has been working with AMR to RFP for a new investment firm to manage the Foundation’s reserves not presently invested in a fidelity account. Two firms have been identified, and the Board will be reviewing these at its upcoming meeting. The hope is that the firm will help the Foundation develop an investment policy and outline short- and long-term investment strategies. This will also lay the groundwork for the AAES and the Foundation to develop an MOU regarding any money that AAES may wish to send to the Foundation to invest.
The Foundation is focused on clarifying the relationship with the AAES. AAESF has been working with the AAES Treasurer on a joint fund raising strategy for both organizations for the upcoming 40th anniversary, and how the two organizations can work together to raise money. It is our goal to raise the remaining $400,000 to allow us to reach the $1 million mark by the time of the 40th anniversary of the AAES next year. A task force of 11 individuals has been created to begin outlining goals and initiatives. In the near future, we will have more information on what are now tentative plans for two new historical lectures and additional funding for the Orlo Clark Lectureship. Information regarding our joint fund-raising strategy will be made available to the members in the very near future.

Finally, the 2018 budget with AMR was approved back in November 2017.

This is an exciting time for the AAES and the Foundation, and we hope that everyone will participate in achieving our goal over the next 12 months. Wishing all of you a wonderful summer.

Geoffrey Thompson, M.D.
Chair, AAES Foundation

Update from the Thyroidectomy Guidelines Task Force
Kepal N. Patel, MD, FACS

In 2016 the AAES leadership approved the development of practice guidelines for best-conduct adult thyroid surgery. By August 2016 a 19-person multidisciplinary writing group was assembled with broad-based expertise in endocrinology, pathology and surgery, co-chaired by Drs. Sally Carty and Chris McHenry.

Subcommittees of 4-8 persons were formed for each of the 20 guideline topics based on relevant expertise and balancing of author responsibilities without conflict of interest. Led in each case by a primary author the subcommittees formally reviewed the literature to prepare topic outlines and draft text, which were discussed, revised, and re-discussed in detail by the entire group during regular teleconferences and via email.

We are excited to report that the progress has been great and a manuscript draft for review and comments by the AAES membership should be available in Fall of 2018. Please look out for this announcement from the AAES. The planned submission for publication of the guidelines will be late Fall or early Winter 2018.

The AAES needs to continue to be leaders and educators in our field of expertise, and so we would like to say thank you to our leadership and members for their support of the guidelines and the committee itself.

Commission on Cancer Update
Jennifer Rosen, MD & Reese Randle, MD

The Commission on Cancer (CoC), established by the American College of Surgeons in 1922, is a multidisciplinary association dedicated to monitoring the quality of care and improving the outcomes of cancer patients through prevention, research, and education.

The AAES successfully applied to join the Commission on Cancer (CoC) as a member organization earlier this spring. Our desire for representation in the CoC is in accordance with our organizational goal of promoting the best treatments for endocrine diseases, and collaboration with the Commission will expand our capabilities in this crucial area.
the CoC should help us affect a greater impact on an even wider scale. On a rotating basis, the AAES will appoint one member and one alternate to serve 3 year terms as representatives of our organization to the CoC. We are currently drafting a list of action items to review with the AAES council and subsequently present to the CoC as the beginning of an ongoing effort to champion standards for management and evaluation of endocrine malignancy.

2019 Local Arrangements Chair
Michael Yeh, MD

My UCLA colleagues and I are thrilled to welcome you to the 40th Annual AAES meeting to be held in Los Angeles, California at the beautiful seaside Fairmont Miramar Hotel from April 7-9, 2019. Though plans for the upcoming meeting are just starting to form, we hope to bring you a "resort style" atmosphere and agenda to allow everyone to enjoy the sun, the sand, and other local attractions in addition to the exceptional intellectual and collegial interactions that are the signature of the AAES. We have chosen the location carefully such that a virtually endless array of food and entertainment options may be found within walking distance of the conference hotel.

I hope you will all attend with your families, and encourage you to both come early and stay late so as to take full advantage of your visit to beautiful Southern California.

In Memoriam: Dr. Jan Erik Varhaug

On December 14, 2017 we learned of the passing of our fellow endocrine surgical colleague, Professor Jan Erik Varhaug, at the age of 75.

Dr. Varhaug served as an endocrine surgeon and professor at Haukeland University Hospital, Bergen, Norway for several decades before retiring five years ago. He was a valued member of the IAES. He contributed significantly, both nationally and internationally, to the field of endocrine surgery. His friendly and personal approach,
combined with his extensive clinical knowledge, experience and his operative skills, were valued greatly by all his friends and fellow surgeons, and patients alike. He will be missed. Our thoughts, prayers and condolences go out to his family at this time.

Endocrine Surgery Reviews

Patient Age-Associated Mortality Risk Is Differentiated by BRAF V600E Status in Papillary Thyroid Cancer


Reviewer:
Iuliana Bobanga, MD, Cleveland Clinic

In Brief
Numerous studies have confirmed the unique prognostic role of patient age in papillary thyroid cancer (PTC), starting with Crile and Hazard in 1953, who described the unfavorable prognosis of advanced patient age at diagnosis.1 Unlike any other cancer, patient age is incorporated in the AJCC staging system for papillary thyroid cancer as a staging dichotomization at 55 years of age.2 However, little is understood of the particular reasons why age is such a strong adverse prognostic factor in PTC. A recent analysis by Adam et al of 31,802 patients with PTC in the SEER database evaluated cancer-specific mortality at 10 years and found a linear relationship between patient age and death from PTC without an age cutoff demarcating a survival difference, challenging the current staging system of PTC.3

In addition to age and other tumor characteristics, the presence of the BRAF V600E mutation has been well known to be an oncogenic driver of PTC, associated with increased recurrence and cancer-related mortality. However, this association is not independent of aggressive tumor features.4 BRAF V600E is also associated with older patient age at diagnosis and occurs in approximately 45% of patients with PTC.4, 5 The present study by Shen et al seeks to evaluate whether patient age at diagnosis is a prognostic factor for all patients with PTC, or whether BRAF V600E receptor status alters the prognostic utility of age in cancer-specific mortality.6

Shen et al conducted a comparative study of the relationship between patient age at diagnosis of PTC and their BRAF V600E status in a large multicenter cohort of patients (2,638 patients at 11 medical centers in six countries). The primary outcome measure was PTC-specific mortality - "death as a result of incurable PTC disease that invaded and compromised vital organs, causing the patient to die". The patients were divided in two groups: patients with wild-type BRAF (n=1,524) and patients with BRAF V600E mutation (n=1,094). Twenty patients were excluded due to failed BRAF genetic testing. A separate sub-analysis was carried out for patients with conventional PTC (CPTC), with 996 patient with wild-type BRAF and 883 patients with BRAF V600E. All patients received conventional treatment, including total or near-total thyroidectomy and other treatments such as radioactive iodine ablation as clinically indicated. The BRAF mutation status was determined after patients were surgically and medically treated and did not affect management decisions. The median follow-up time was 58 months.

The results were strikingly distinct between the two groups based on BRAF mutation status. There was a linear relationship between patient age and PTC-specific mortality in all patients when the cohort was taken together, but a steeper linear relationship in patients with BRAF V600E. However, in patients with wild-type BRAF,
PTC-specific mortality remained flat with increasing patient age. Thus, the age-associated mortality risk in PTC patients without a BRAF V600E mutation was completely lost, making age not a significant risk factor in this patient population. The analysis was adjusted for patient sex, tumor size, extrathyroidal extension, lymph node metastasis, distant metastasis and radioactive iodine treatment, and the linear relationship in the BRAF V600E group persisted. When the same analysis was performed for CPTC patients with wild-type BRAF versus CPTC patients with BRAF V600E, the results mirrored those for the entire cohort, showing a similar BRAF-V600E-dependent relationship between age at diagnosis and increased mortality risk. Age was not a risk factor for worse prognosis in CPTC patients with wild-type BRAF.

Critique
This large multicenter cohort study by Shen et al brings a significant contribution to the understanding of age as a mortality risk factor in patients with PTC. It essentially shows that the increased risk of advanced age in PTC is completely BRAFV600E-dependent. If patients do not have this mutation, age is not a risk factor for poor prognosis. Importantly, it also shows a linear relationship between increasing age and PTC-specific mortality in patients with BRAF V600E mutations, without a dichotomous cutoff age. These two conclusions challenge the current AJCC staging system for PTC, which uses an age cutoff of 55 years for higher stage and currently does not incorporate BRAF mutation status. This study also has implications in how aggressively patients with PTC should be treated based on age and BRAF mutation status. Older patients with wild-type BRAF status may be able to avoid more aggressive treatment as their outcome is similar to younger patients with wild-type BRAF status. However, the ability to perform BRAF genetic testing on all patients with PTC will be extremely costly and challenging, and many years away from widespread implementation.

A limitation of this study is the lack of evaluating other mutations, such as the TERT promoter mutation, which also confers a poor prognosis to PTC. The TERT promoter mutation is known to coexist with BRAF V600E mutations and is more common in older patients, and could confer a confounding effect on mortality risk. Another limitation is the absence of incorporating other thyroid cancer, such as follicular and Hurthle cell cancer that are also stages based on age in this study. Although this was a robust cohort size, due to the low mortality risk of thyroid cancer, a larger cohort and longer follow-up duration may elucidate the effect of multiple molecular markers on age as a prognostic factor for various subtypes of thyroid cancer.

Future Directions
While the association between BRAFV600E and age is further elucidated by this study, the underlying mechanism is not well understood. Particularly why older patients with BRAFV600E do worse than younger patients with the same mutation remains to be clarified. Future studies are needed to confirm the results found by Shen et al, and would also include a larger variety of thyroid cancers and have longer follow-up duration.

References:

Additional High Yield Reading:

Effect of parathyroidectomy on quality of life and non-specific symptoms in normocalcaemic primary hyperparathyroidism


Reviewer:
Denise Lee, Columbia University

In Brief
Normocalcemic primary hyperparathyroidism (NcPHPT) is a clinical entity that has been increasingly recognized as a biochemical variant of PHPT where parathyroid hormone (PTH) levels are elevated but calcium levels remain normal. To establish this diagnosis, causes of secondary hyperparathyroidism (vitamin D deficiency, medications, malabsorption syndromes) must be ruled out (1). While some consider NcPHPT a milder form of PHPT, the pathophysiology and natural history of this clinical phenotype remains relatively unknown and has been highlighted as an important topic for future studies in the fourth international workshop guidelines for asymptomatic PHPT (2). Importantly, the best practice management of patients with NcPHPT and those with mild PHPT who do not meet surgical criteria is also uncertain. Although many patients with PHPT complain of non-specific symptoms such as abdominal pain, polyuria, fatigue and muscle aches, the presence of these non-specific symptoms has not been established as a criterion for undergoing surgery. It remains unknown if these symptoms improve after parathyroidectomy in patients with NcPHPT or mild PHPT.

In this study, Bannani and colleagues sought to understand: 1) if non-specific symptoms often identified in patients with classic PHPT are also present in those with NcPHPT, 2) if present, how they might affect quality of life (QoL) and 3) if parathyroidectomy could improve and ameliorate these symptoms and patient QoL. Over three years the authors prospectively enrolled 114 patients with mild PHPT and classified them as either NcPHPT (serum calcium at the upper limit of normal with elevated PTH) or mildly hypercalcemic (Hc-m-PHPT, serum calcium ranging from 10.4-11.4mg/dL with elevated PTH). All patients underwent a parathyroidectomy and were evaluated before surgery, and at 3, 6, and 12 months after parathyroidectomy. At each time point laboratory data was collected (total serum calcium, serum phosphate, creatinine, PTH, 25-OH vitamin D) and two self-administered questionnaires were performed. The first questionnaire, Short Form 36 questionnaire (SF-36-v2), assessed QoL using eight health concepts and obtained from this two summary outcomes: the physical component summary (PCS) and mental component summary (MCS). The second questionnaire assessed for twenty-five non-specific physical and neurocognitive symptoms associated with PHPT.

The authors found that at baseline the only significant preoperative difference between the NcPHPT and Hc-m-PHPT groups was the serum calcium level. There was no difference in MCS or PCS scores and no difference in the frequency of nonspecific symptoms. Postoperatively the overall cure rate was 98.2% at 6 months
and 25-OH vitamin D levels improved significantly for the Hc-m-PHPT group at 3 months but remained unchanged in the NcPHPT group. After surgery, the NcPHPT group had significant improvement in QoL in three of eight aspects of the SF-36v2 at 3 months, one of eight at 6 months and three of eight at 1 year. However, after Bonferroni correction there was no significant improvement in any of the eight aspects at either 3 or 6 months and only the role (physical aspect) was improved at one year. After surgery, the Hc-m-PHPT showed significant improvement in almost all of the eight aspects at 3, 6 months and 1 year, even after Bonferroni correction. Regarding non-specific symptoms, more patients in the Hc-m-PHPT improved than in the NcPHPT group.

Critique
This study from Bannani and colleagues investigates an important question regarding the effect of parathyroidectomy on quality of life and non-specific symptoms frequently reported by patients with PHPT. One of the strengths of the study lies in its study design and execution of a multicenter prospective trial using a validated QoL survey. The authors found that patients with NcPHPT and Hc-m-PHPT both reported non-specific complaints, such as bone and joint pain, muscle weakness and anxiety. This is data that has not been previously reported and adds valuable insight into a disease process that has only recently become increasingly studied. After parathyroidectomy, patients in both groups reported variable QoL and non-specific symptom improvement which is consistent with studies investigating hypercalcemic PHPT patients.

Little remains known about the benefits of parathyroidectomy for patients with Nc-PHPT. While well-established guidelines exist for the surgical management of typical hypercalcemic PHPT, there is currently a paucity of data available to help guide practitioners on when or whether parathyroidectomy is beneficial for patients with NcPHPT. Among the few studies that have investigated therapies for NcPHPT patients, Koumakis and colleagues have reported an improvement in bone mineral density for patients with NcPHPT after parathyroidectomy (3). This multicenter prospective trial by Bannani and colleagues significantly adds to the growing literature on the symptoms and treatment effect of surgery in NcPHPT patients.

However, there are limitations to this study, which include the lack of an untreated control group to better compare the effectiveness of surgery. Also, ionized calcium levels were intentionally excluded from the laboratory assessment. Current criteria for defining NcPHPT include ionized calcium as a metric to be evaluated as it can be elevated while total serum calcium levels remain normal. This inclusion of ionized calcium levels may have reclassified some patients as having mild rather than normocalcemic PHPT, thus altering the reported outcomes.

References:

Additional High Yield Reading:
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