Meet the Professor

Dr. Varun Puri: decision analysis works to compare therapies when randomized clinical trials cannot

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Editor's note

Decision making in clinical practice is often based on a series of careful analyses of benefits and harms associated with different treatment options. These decisions, usually made under competing priorities, limited resources and information, are critical as they would directly influence patients' long-term consequences. Decision analysis is thus frequently used by clinicians who apply evidence-based medicine to achieve the best possible decision given a specific clinical situation.

In the practice of Dr. Varun Puri, a thoracic surgeon and the Associate Professor of Surgery at Washington University School of Medicine, decision analysis is repeatedly used in several of his studies to compare different therapies, such as stereotactic radiation therapy versus surgical resections in early stage lung cancer, and combined chemoradiation therapy versus trimodality therapy in patients with stage III lung cancer. In the following interview, we will have a more in-depth look at his research in the field of lung and esophageal cancers, and how he used decision analysis to address different clinical paradoxes.

Expert's introduction

Varun Puri, MD, MSCI, currently serves as the Associate Professor of Surgery, Division of Cardiothoracic Surgery, Washington University School of Medicine, St. Louis, MO. Clinically, he is a thoracic surgeon specializing in lung and esophageal cancers and Barrett's esophagus (*Figure 1*).

Dr. Puri's research is focused on using large databases to study clinical problems in lung and esophageal cancer; determining risk factors predictive of occult mediastinal lymph node involvement in patients with early non-small cell lung cancer, and evaluating hand-held spirometry as an alternative to laboratory based volume-displacement spirometry in a low-risk population undergoing lung resection. His work has been funded by various organizations including the National Institutes of Health.

Figure 1 Dr. Varun Puri.

Interview

JTD: What do you think are the critical issues facing the field of lung and esophageal cancers?

Dr. Puri: The critical issues facing the field of lung cancer are somewhat distinct between early stage lung cancer and more advanced disease. In the field of early stage lung cancer, where surgical management has generally been regarded the gold standard, the advent of stereotactic radiation therapy has provided a suitable alternative in the high-risk patient category. Future studies will more clearly define the population where non-operative treatment is preferable. In the field of advanced lung cancer, the rapid evolution of immunotherapy and other forms of systemic therapy have provided an important avenue for effective therapy and improving progression free survival. Nevertheless, surgical resection still remains an option in patients with stage III disease and more effective systemic therapy may make it a more viable option in selected patients. Similarly in patients with oligometastatic lung cancer, small clinical trials have shown a role for local

therapy including surgery. This is an area that needs to be explored further.

From a surgical perspective, the most important issue in the field of esophageal cancer is appropriate patient selection for trimodality therapy. As we very well know, between 20% and 35% of individuals with esophageal adenocarcinoma have complete pathologic response in their resected specimens. If there were reliable and reproducible tests to predict this before surgical resection, then one would potentially be able to avoid surgery in this patient population. Although a combination of molecular and radiologic testing has been shown to have modest degree of reliability in predicting complete pathologic response, the failure rates of these tests are significant and would deny many patients potentially curative therapy.

JTD: What is decision analysis? How can it be adopted to answer various clinical questions?

Dr. Puri: Decision analysis refers to a systematic, quantitative and interactive approach to addressing and evaluating important choices. Decision analysis provides an algorithm whereby one can compare two or more alternative therapies for any clinical situation and assess the downstream consequences of each therapy based upon probabilities that are derived from clinical trials or published medical literature. It is important however to ensure that the virtual patient for whom decision analysis is employed, is equally eligible for the alternative therapies that are being considered.

Decision analysis has been employed in several prior studies to compare therapies when head to head comparisons in randomized clinical trials are not possible. As an example, our group has previously compared stereotactic radiation therapy and surgical resections in early stage lung cancer, as well as combined chemoradiation therapy versus trimodality therapy in patients with stage III lung cancer. These are areas where clinical trials have failed to provide adequate evidence and decision making processes in clinical medicine can be informed by such studies.

JTD: What makes the treatment of T2N0 esophageal cancer so complex? What role does decision analysis play in the treatment of this cancer?

Dr. Puri: T2N0 esophageal cancer represents a disease process where there is significant uncertainty in the clinical stage at diagnosis. The vast majority of patients who are diagnosed with clinical T2 N0 cancer based upon endoscopic ultrasound and imaging studies do not have pathologic T2N0 disease. This makes the preoperative treatment planning challenging. If patients are expected to have more advanced stage disease, induction chemoradiation therapy would be an important consideration. On the other hand, a lower pathologic stage suggests that preoperative induction therapy would not have been necessary. Using decision analysis, our study concluded that "*The optimal treatment strategy for cT2N0 esophageal cancer depends on the accuracy of endoscopic ultrasound staging. High-risk features that confer increased probability of upstaging can inform clinical decision making to recommend induction chemoradiation for select cT2N0 patients*."

JTD: Would you introduce us to a recent research project?

Dr. Puri: Our group has recently conducted a pilot study whereby we evaluated the role of oral decontamination in patients undergoing elective lung operations. We noticed that there is potentially lower likelihood of postoperative pneumonia in patients undergoing oral decontamination. This study has allowed us to assess the estimated incidence of postoperative pneumonia with and without oral decontamination therapy. Our study has also shown that there is excellent adherence to this simple oral decontamination protocol. We are in the process of designing a multicenter trial and will seek NIH funding for that study.

JTD: Did you come across any bottleneck throughout your research career? Is there anything memorable you would like to share?

Dr. Puri: A significant hurdle in any research initiative is the initial time and effort that it takes to assemble a research team that is effective, productive, and collegial. I strongly believe that this initial effort is time well spent for any researcher. What has been most noteworthy for our research team has been the many significant contributions that have come from young medical and graduate students who have been involved in many of our research lab's projects. I am personally grateful to have been able to work with these young researchers.

JTD: As an experienced researcher and professor, what would be your tips to young researchers who would like to develop their expertise/career in your field?

Dr. Puri: From a research perspective, I have primarily

two suggestions to young researchers. One, try and answer questions which you think will be of importance to the field today, as well as 5–10 years in the future. This perspective will allow you to pursue and generate information that will remain relevant as technological changes occur in the field of thoracic surgery. The second recommendation is to ensure that your research questions are hypothesis driven. It is tempting, with the availability of large datasets, to go on a datamining expedition. However, the research findings are far more likely to be meaningful and clinical applicable, if they are directed by a testable hypothesis. Finally, one cannot overstate the importance of a team approach to research and one must always strive to be a part of a highly functioning and effective team.

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Footnote

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