Anesthesiologists play a crucial role in the improvement of the outcome of surgical patients with their decision making on preoperative optimization, intraoperative management and postoperative care. The evolution of this role has brought anesthesiologists to a broader perspective, wherein interventions within the purview of anesthesiologists may reduce the complications from both surgical stress and underlying diseases (1). For example, timing of antibiotics, maintenance of normothermia, blood transfusion, and perioperative medication management can have a significant impact on the overall outcomes of surgical patients (2). In an optimal world, the clinical decisions made by anesthesiologists to provide perioperative care and improve outcomes will be based on objective clinical evidence from well-designed clinical trials. How to best utilize existing evidence to provide high value for an individual patient in a particular clinical setting is a challenge.

A well-known example of evidence applied to perioperative practice by anesthesiologists is the role of beta-blocker therapy to mitigate the risk of perioperative cardiovascular complications (3). As cogently outlined by Neuman et al., clinical guidelines for perioperative beta-blocker therapy have had a long and controversial history even though they are rooted in what appeared to be robust clinical evidence (4). While the beta-blockade story continues to unfold, the advent of ‘big data’ research methodologies has revealed that non-cardiac morbidity (e.g., pulmonary and gastrointestinal complications) is significant and affords an opportunity for high impact quality improvement efforts (5). However, for perioperative care, ‘best practice’ for many fundamental interventions remains to be adequately evaluated or supported by evidence. Examples include ventilation strategy for low-risk surgical patients (6), fluid therapy for perioperative intravascular volume maintenance, analgesic approach for surgical pain control, and anesthetic technique in patients at risk for perioperative cognitive decline. Evidence is gradually being produced. A recent multicenter randomized controlled trial reported that ventilation with high tidal volume might cause lung injury in surgical patients with relatively normal lungs (7). As such data is published, clinicians are left wondering: should the new findings be applied to my patient in the operating room (OR) today, or should I wait for more, stronger, and more directly applicable evidence?

The source and quality of the clinical evidence is an important factor. There are heated debates over what constitutes legitimate or best evidence. GRADE system is one of the most commonly used rating systems currently. There are two grades of recommendations including ‘strong’ and ‘weak’ in the system, and the quality of evidence is classified to four levels (Table) (8, 9). Among the evidence provided by clinical studies, systematic review (especially meta-analysis) and randomized clinical trials (RCTs) are ranked as the highest-quality evidence available in clinical practice (8, 9). For individual experimental study, RCTs, designed to determine whether an intervention works under certain conditions, are conducted to prove efficacy. The well-defined inclusion and exclusion criteria as well as randomly assigning one patient pool to an intervention and another patient pool to non-intervention (or placebo) minimize the biases from the confounding factors (particularly unknown confounding factors). The strict protocol of RCTs, following the regulations such as Good Clinical Practice (GCP), assures the very high internal validity of the trials. This does not necessarily lead to high external validity, which is the validity of the evidence from the trial when applied to individuals among the defined population but not recruited in the trial. For example,
in the study by Futier et al. just mentioned above, the strategy of a high tidal volume with no positive end-expiratory pressure (PEEP) might be potentially harmful while the multifaceted strategy with a low tidal volume, PEEP and recruitment maneuvers during surgery might reduce postoperative complications (7). Whether a low tidal volume, PEEP, or recruitment be used safely in our clinical practice as the research suggested? In another later study published on Lancet by The PROVE Network Investigators argued that a strategy of high level of PEEP combined with recruitment manoeuvres did not protect against postoperative pulmonary complications, while a low tidal volume and low PEEP (≤2 cm H2O) without recruitment manoeuvres should be the recommended strategy of perioperative ventilation (10). Beyond that, a ventilation strategy studied in normal weight patients is not necessarily generalizable to the obese population. In addition, the implementation of evidence, even from well-designed trials, in a bigger or different population compared to that of the studies should be reevaluated with the consideration of the baseline risk-benefit profile of the patients of interest.

RCTs in the cardiovascular field such as the studies of beta-blockers, statins, coronary revascularization and thermal management have changed the clinical practice of anesthesiologists with outcome improvements and higher value care. However, some recent studies on beta-blockers in non-cardiac surgery such as POISE and DECREASE demonstrate the importance of protocol design and sample size for solid evidence (11, 12). The utility of small-scale studies is often called into question since large study size theoretically provides more to determine less common events such as perioperative stroke and may be less vulnerable to hidden sources of bias (13). Additionally, the quality of the implementation of the study can call into question the validity of the results (14).

Another common study design is the cohort study. Cohort studies usually have a sample size sufficient enough to determine the presence of rare associations and can be retrospective or prospective. A variety of statistical techniques are used to try to identify and control for confounding factors in the cohort groups. For example a recent cohort study of 15,000 United Sates surgical patients with either diagnosed obstructive sleep apnea (OSA) or a positive bedside sleep apnea screen failed to demonstrate an association with 30-day or 1-year postoperative mortality (15). The authors point out that such studies contradict the widely held assumption of OSA and increased perioperative risk and help to guide the direction of future research endeavors on the topic. The OSA study was limited since it was a single center trial. This suggests the need for a multicenter trial which has the advantage of a large size of sample, variety in geographic location, the possible recruitment of a wide range of population groups and the comparison of results among centers. All of these enhance the generalizability of the study. Geographically dispersed multicenter trials can evaluate a finding which will vary significantly between population groups with different genetic, environmental, and ethnic or cultural backgrounds.

Analysis of administrative databases such as Medicare claims data in the United States and The National Surgical Quality Improvement Program (NSQIP, http://site.acsnsqip.org/) offers another important approach to studying effectiveness of an intervention in clinical practice. The use of ‘big data’ analytics to improve health is of growing relevance to all practitioners and certainly in the perioperative realm (e.g. Institute of Medicine, Health Data Initiative, https://www.iom.edu/Activities/PublicHealth/HealthData.aspx). For example, in a Medicare claims cohort study of 57,000 patients in 50 New York hospitals, Neuman et al. (16) demonstrated reduced perioperative complications with regional anesthesia as opposed to general anesthesia in patients undergoing surgery for hip fracture.

Clinical guidelines are developed through identifying, synthe-

Table. Quality of Evidence and Definitions (GRADE).

<table>
<thead>
<tr>
<th>Quality</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High quality</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect</td>
</tr>
<tr>
<td>Moderate quality</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate</td>
</tr>
<tr>
<td>Low quality</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate</td>
</tr>
<tr>
<td>Very low quality</td>
<td>Any estimate of effect is very uncertain</td>
</tr>
</tbody>
</table>
which was emphasized in practice guidelines 2013, and succeeded in dealing with the emergency scenario (19, 20). A problem is when guidelines are desirable but the available evidence is non-existence or of low-quality. One can pose the question: does consensus expert opinion alone warrant the dissemination of guidelines in an effort to decrease variation in care or should guidelines only be written when high quality evidence is available. A recent study of American College of Cardiology guidelines demonstrated that those lacking strong prospective RCTs based support ultimately had the least durability and highest likelihood of being modified or downgraded on subsequent revision (16).

This leads us to the conclusion that practice should also be individualized when referred to single patient or population of certain characters if optimal outcomes are desired. Since the inclusive criteria from the clinical trials may not be the same as the characteristics of the patients actually being treated, evidence from these trials are not necessarily applicable to your patients and the effectiveness of the interventions may not be as high. A combination of clinical findings, prior experience in the localized setting, and the application of the literature evidence will help us determine the benefit and risk and lead to an action. This may be particularly important when substantial ethnic and genetic differences exist between the study population and the real world population. For example, in Chinese patients, the prevalence of hypercoagulable state and associated complications such as deep venous thrombosis (DVT) appears to be lower than that in Western populations (21). Under such circumstances the applicability of studies such as POISE-2 (22), which examined the relative risk of thrombosis versus bleeding with perioperative aspirin in surgical patients, may be less in the local Chinese population.

In applying evidence, it is also important that for some individuals the probability and extent of disease is less precise and testing can potentially have value in determining if action should be taken. A positive test may raise the probability of a certain disease or complications while a negative test would lower the probability and obviate any need for action. For example, for patients with known risk factors for coronary disease undergoing non-cardiovascular surgery, further testing such as computed tomography angiography (CTA) or coronary angiography (CAG) may help with decision making. A recent example of assessing risk and utilizing clinical and laboratory information to dictate subsequent care is the use of the Revised Cardiac Risk Index (RCRI). The RCRI was employed in several studies to define a population at risk that was subsequently randomized to two different treatment regimens such as coronary angiography for potential randomization to medical versus revascularization therapy in the Coronary Artery Revascularization Project (CARP) (23). Additionally, the RCRI has been utilized to determine the potential benefit or risk of perioperative beta-blocker or statin therapy in several studies utilizing adminis-
The quality and robustness of the evidence from clinical studies should be confirmed before finally applying them to change current practice. A recent multicenter study on the protective ventilation with low tidal volume has concluded that low tidal volume should be recommended to reduce lung injury in surgical patients with relatively healthy lungs (7). This evidence seems to be promising as protective ventilation with low tidal volume is an inexpensive intervention without important adverse effect. However, changing practice based on a single clinical trial is not reasonable. The critically ill patients in intensive care unit (ICU) with acute respiratory distress syndrome (ARDS) showing benefit from protective ventilation have a different overall risk-benefit profile compared to surgical patients. Theoretically a population under much lower risk from different ventilation strategies (e.g. surgical patients) will likely benefit less from the same protective intervention compared to the patients with ARDS who already have lung injury. Another example is that results from high risk coronary heart disease (CHD) patients regarding the protective effect from beta-blocker are not necessarily applicable for low-risk patients who actually may experience a higher risk of stroke when started on a perioperative beta-blocker (11, 25).

Patient preferences should also be incorporated into decision making. This is most important in intermediate risk patients and procedures. Patients themselves are the most important component of the care. The optimal decision for patients relies on the value of a specific outcome by a certain patient, which can be very different from patient to patient. Under these circumstances when evidence provides no clear direction, patient preferences should be dominant (26).

In summary, utilizing evidence in the perioperative period by anesthesiologists should result in improvement in patient outcomes. The body of evidence by which we make critical decisions needs to be enhanced. The standardization of perioperative care based on clinical data such as guidelines, and the individualization of perioperative management in the actual practice based on the local environment and personalized benefit-risk evaluation, are the two sides of the same coin. In most cases guidelines will provide general recommendation. In order to achieve the best outcome for the patient, anesthesiologists should understand how to evaluate clinical evidence with respect to the appropriate population and protocols in order to effectively apply the data to a given clinical situation.

From ‘Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China; P’Reelman School of Medicine, University of Pennsylvania, Philadelphia, USA. Correspondence to Dr. Lee A. Fleisher at leefleisher@uphs.upenn.edu. All authors have no financial support and potential conflict of interest for this work. Citation: Jing Zhou, Joshua Atkins, and Lee A. Fleisher. The application of evidence by anesthesiologists to provide perioperative care of better value. J Anesth Periop Med 2015; 2: 107-10.