Difficult Decisions in Surgery:
An Evidence-Based Approach

Peter Angelos · Raymon H. Grogan
Editors

Difficult Decisions in Endocrine Surgery

An Evidence-Based Approach

Springer

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The complexity of decision making in any kind of surgery is growing exponentially. As new technology is introduced, physicians from nonsurgical specialties offer alternative and competing therapies for what was once the exclusive province of the surgeon. In addition, there is increasing knowledge regarding the efficacy of traditional surgical therapies. How to select among these varied and complex approaches is becoming increasingly difficult. These multi-authored books will contain brief chapters, each of which will be devoted to one or two specific questions or decisions that are difficult or controversial. They are intended as current and timely reference sources for practicing surgeons, surgeons in training, and educators that describe the recommended ideal approach, rather than customary care, in selected clinical situations.

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Dr. Grogan:
I dedicate this book to my wife Yuemi and my two beautiful girls Ivy and Emery. Thank you Yuemi for supporting me day in and day out even though I spend so many hours away from home. And thank you Ivy and Emery for being my own personal "Fountain of Youth." You truly are a joy, an inspiration, and a daily source of pride and motivation.

Dr. Angelos:
I dedicate this book to my wife Grace without whose support none of my efforts would have been possible and to my children. Without Audrey, Christian, Meghan, and son-in-law Zach, life would not be nearly as exciting nor as much fun. Thank you all for your understanding and support.

Acknowledgements

There are several people who helped make this book possible. First and foremost, we would like to say thank you to our friend and colleague Dr. Edwin Kaplan. We both have benefited tremendously from the wisdom, knowledge, and camaraderie of working next to Dr. Kaplan on a daily basis. His inquisitive nature and seemingly bottomless wealth of knowledge on the subject of endocrine surgery has certainly changed the way we (and many people throughout the world) practice. Without his friendship over the years it is safe to say that we would not be the same surgeons we are today, and thus, this book would be a different book.

We would also like to thank the unseen heroes who work hard day in and day out taking care of our patients and practice, because without them we truly would not have the time or energy to pursue an academic endeavor such as this book. Ms. Pat Schaddelee our administrative assistant who basically does everything for us, Mrs. Sandra Frausto our RN and practice manager who is the face of our practice for our patients, and Mrs. Joly Raju our nurse practitioner who knows more about endocrine surgery than many endocrinologists we know.

Finally, we would also like to say thank you to all the endocrine surgery fellows and research fellows we have worked with over the years, because again it is their hard work and dedication that help to make academic pursuits like this possible. But more than that it is the fellows that help shape the way we perceive and think of the future of endocrine surgery as a specialty, and their influence has helped shape the content of this book.

Introduction

> The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research—From "Evidence based medicine, what it is and what it isn't" BMJ Jan 13 1996 Volume 312

What Is a Difficult Decision?

Life is a constant stream of decision making. From the time we wake up until the time we go to bed, we are continually making decisions. Every action taken, every movement, every thought has derived in some way from the decision-making process. Decision making is so essential to everyday function that it seems like much of it happens without our consciously thinking about it. But have you ever stopped to think about what a decision is and how it is derived? When you stop to consider this for a moment, you realize that what seems like something simple and mundane, the act of making a choice, is actually quite complex. So complex that there are entire psychology departments, societies, and scientific journals dedicated to studying and understanding human decision making. For the context of this book, however, let us consider a simple definition. In essence, decision making is the process of selecting a course of action from among multiple alternative possibilities. The final result of this process being a choice that will ultimately lead to future consequences. In medical decision making, it is these future consequences that we are consciously and subconsciously weighing every time we give our advice or opinion to our patients. Decision making becomes difficult when there is uncertainty regarding the type or magnitude of the consequences of each alternative being weighed. The more uncertainty, or the bigger the possible consequence, the more difficult the decision. Uncertainty is inherent in the medical decision-making process. We as physicians expect that our tests are not perfect, good outcomes are not always guaranteed, and the risks and benefits of our interventions vary based on circumstance. After all, it often seems as if the whole point of learning about sensitivity, specificity, and receiver operator curves in medical school is to remind us of the fact that there is still a certain amount of "art" in the science of medicine.

What Is This Book About Anyway?

It is from this idea that a lack of information leads to difficult decisions that this book *Difficult Decisions in Endocrine Surgery* was created. We started with a simple premise, to identify clinical scenarios that we see in our academic endocrine surgery practice that made us pause for a minute and think "what in the world *are* the evidence-based data on *that*?" Fortunately for us as editors of this book, there is no paucity of unusual, rare, and interesting cases that come through a busy academic endocrine surgery practice. That aspect of endocrine surgery is in part what makes it such an interesting clinical practice and what drives so many interesting research questions. Aside from the rare and unusual we also felt that to keep the book contemporary and useful on a broader level it was important to include chapters on things that might be more common, but are still controversial. Once the questions were identified, we looked through available literature as well as past meetings of the American Association of Endocrine Surgeons to find our expert chapter authors. We asked these authors to use a strict set of guidelines to write evidence-based medicine chapters on each topic. The goal being to provide the reader with the highest level of evidence possible to allow for clinical decision making. You can think of this book almost as a premade literature search combined with an expert mentor giving his or her own take on that literature. At the time of the writing of this book, there really is no additional scientific evidence available on most of these topics outside of what you will find synthesized here.

What Is Evidence-Based Medicine Really?

A common theme you will see throughout this book is a lack of good, objective level 1 evidence for many of the topics being discussed. Using the definition of a "Difficult Decision" that we outlined above, it was inevitable that we would come up with a set of clinical scenarios that did not have much evidence to support their treatment or care. So you might reasonably ask, is this book then an evidence-based book? We would argue that yes, in fact, this is an evidence-based book of a high quality. We believe this to be the case because the meaning and purpose behind the idea of "evidence-based medicine" is often misunderstood. Evidence-based medicine is not a mechanical following of practice guidelines. As explained in an editorial by Dr. David Sackett, one of the pioneers and founders of the evidence-based medicine movement, "The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research." In endocrine surgery, because there are many things that are unusual and rare we deal daily with cases and scenarios that do not have high levels of research-based evidence. In these cases, we can still practice evidence-based medicine, but we do this by integrating what little evidence is known with our own clinical experience along with the clinical expertise of those among us who have the most experience dealing with these situations. In this way, we learn and grow as individual practitioners and expand the broader field of endocrine surgery. We hope

you find this book informative and useful, as well as helpful for your patients. We also hope that you take the lack of evidence presented in this book not as a negative but as a positive motivator to continue to expand your own personal research endeavors, as well as those of the entire endocrine surgery community. It is the basic inquisitive nature that is at the core of what drives so many of the most important clinical research studies. If this book leaves you with more questions than answers, then perhaps, counterintuitively, we have done our job.

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Abbreviations

Misc

3HPT	Tertiary hyperparathyroidism
4DCT	Four-dimensional computed tomography
5-FU	Fluorouracil

A

AACE	American Association of Clinical Endocrinologists
AAES	American Association of Endocrine Surgeons
ACC	Adrenocortical carcinoma
ACS-NSQIP	American College of Surgeons' National Surgical Quality Improvement Program
ACTH	Adrenocorticotropic hormone
AIMAH	ACTH-independent macronodular adrenal hyperplasia
APA	Aldosterone-producing adenoma
ARR	Aldosterone-to-renin ratio
ATA	American Thyroid Association
ATC	Anaplastic thyroid cancer
AUC	Area under the curve
AUS	Atypia of undetermined significance
AVS	Adrenal vein sampling or adrenal venous sampling

B

BAH	Bilateral adrenal hyperplasia
BMAH	Bilateral macronodular adrenal hyperplasia
BMD	Bone mineral density
BNE	Bilateral neck exploration

C

CaSR	Calcium-sensing receptor
CDA	Clinical decision analysis
CgA	Chromogranin A
CHPA	Cryopreserved heterotopic parathyroid autotransplantation
CT	Completion thyroidectomy
CT	Computed tomography

D

DFI	Disease-free interval
DFS	Disease-free survival
DXA	Dual-energy X-ray absorptiometry

E

EBM	Evidence-based medicine
EBRT	External beam radiotherapy
ECOG	Eastern Cooperative Oncology Group
EDTA	Ethylenediaminetetra-acetic acid
EGFR	Epidermal growth factor receptor (EGFR)
ENSAT	European Network for the Study of Adrenal Tumor
ESMO	European Society of Medical Oncology
EUS	Endoscopic ultrasound

F

FHH	Familial hypocalciuric hypercalcemia
FIHP	Familial isolated hyperparathyroidism
FIRM-ACT	First international randomized trial in locally advanced and metastatic adrenocortical carcinoma reatment
FLUS	Follicular lesion of undetermined significance
FN	False-negative
FNA	Fine-needle aspiration
FNMTC	Familial non-medullary thyroid cancer
FP	False-positive
FTC	Follicular thyroid carcinoma

G

GAN	Greater auricular nerve
GEC	Gene-expression classifier
GLP-1	Glucagon-like peptide 1 analog
GRADE	Grades of recommendation, assessment, development, and evaluation
GRBAS	Grade, roughness, breathiness, asthenia, and strain
GY	Gray

H

HNR	Harmonics-to-noise ratio
HPF	High-power field
HPT	Primary hyperparathyroidism
HPT-JT	Hyperparathyroidism jaw tumor
HTC	Oncocytic or Hurthle cell variant of FTC
HTN	Hypertension
HypoCa	Hypocalcemia

I

IA	Interarytenoid
ICU	Intensive care unit
IDLE	Indolent lesions of epithelial origin
IHA	Idiopathic aldosteronism
IMRT	Intensity-modulated radiotherapy
IOPTH/IoPTH	Intraoperative parathyroid hormone
IOUS	Intraoperative ultrasound
^{131}I-MIBG	Iodine meta-iodobenzylguanidine
iPTH	Intact PTH
IRI	Immunoreactive insulin
IVC	Inferior vena cava

L

LA	Laparoscopic adrenalectomy
LCA	Lateral cricoarytenoid
LN	Lymph node
LOS	Length of stay
LSP	Less than subtotal parathyroidectomy
LTA	Laparoscopic transperitoneal adrenalectomy

M

MDCT	Multidetector CT
MEN 1	Multiple endocrine neoplasia type 1
MeSH	Medical subject headings
MGD	Multiple gland disease
MIBI	99mTc-sestamibi
MIP	Minimally invasive parathyroidectomy
MR	Mineralocorticoid receptor
MRI	Magnetic resonance imaging
MTC	Medullary thyroid carcinoma
mTOR	Mammalian target of rapamycin
MTNS	McGill thyroid nodule score
MWA	Microwave ablation

N

NANETS	North American Neuroendocrine Tumor Society
NCCN	National Comprehensive Cancer Network
NCDB	National Cancer Database
NED	No evidence of disease
NGS	Next-generation sequencing
NIFT-P	Noninvasive follicular thyroid neoplasm with papillary-like nuclear features
NIH	National Institutes of Health
NIS	Nationwide Inpatient Specimen
NPV	Negative predictive value
NR	Not reported
Ns	Not specified

P

PA	Primary aldosteronism
PAF1	Polymerase II–associated factor 1
PCA	Posterior cricoarytenoid
PCR	Polymerase chain reaction
PDC	Poorly differentiated thyroid carcinoma
PDGF	Platelet-derived growth factor
PDNET	Pancreaticoduodenal neuroendocrine tumors
PEI	Phonation efficiency index
PET-CT	Positron emission tomography–computed tomography
PFS	Progression-free survival
PHP	Primary (chief cell) hyperplasia

pHPT	Persistent hyperparathyroidism
PICO	Population, intervention, comparator, and outcome
PNET	Pancreatic neuroendocrine tumor
PPAR	Peroxisome proliferator-activated receptor
PPNAD	Primary pigmented nodular adrenocortical disease
PPV	Positive predictive value
PRA	Posterior retroperitoneal adrenalectomy
PRO	Patient-reported outcomes
PTC	Papillary thyroid cancer
PTC-FV	Follicular variant of PTC
PTH	Parathyroid hormone
PTHrP	Parathyroid hormone-related peptide
PTMC	Papillary thyroid microcarcinomas
PTX	Parathyroidectomy
PV/SMV	Portal vein/superior mesenteric vein

Q

QALY	Quality-adjusted life years
QOL	Quality of life

R

R	Retrospective
RCT	Randomized controlled trials
RFA	Radiofrequency ablation
RH	Resistant hypertension
rHPT	Recurrent hyperparathyroidism
RLN	Recurrent laryngeal nerve
RPMI	Roswell Park Memorial Institute
RPT	Randomized, prospective trial
RTOG	Radiation Therapy Oncology Group

S

SABR	Stereotactic ablative body radiotherapy
SCIP	Surgical Care Improvement Project
SEER	Surveillance, epidemiology, and end results
SeS	Sestamibi
SF-36	Short form 36
SP	Subtotal parathyroidectomy
SPECT	Single-photon emission computed tomography

SRI	Surgically remediable aldosteronism
SSA	Somatostatin analogue
SSI	Surgical site infections
SSTR	Somatostatin receptors
SUS	Surgeon-performed ultrasound
SV	Splenic vein
SVS	Selective venous sampling

T

TA	Thyroarytenoid
TP/AT	Total parathyroidectomy and autotransplantation
TSH	Thyroid-stimulating hormone
TT	Total thyroidectomies

U

UFC	Urinary free cortisol
UICC	Union for International Cancer Control
US	Ultrasonographic
US FDA	United States Food and Drug Administration
USG	Ultrasonography
USG-FNAC	USG-guided fine-needle aspiration cytology
UTC	Undifferentiated or anaplastic thyroid carcinoma
UTI	Urinary tract infection

V

VEGF	Vascular endothelial growth factor
VFA	Vertebral fracture assessment
VHI	Voice handicap index
VHL	von Hippel-Lindau type 1

W

WHO	World Health Organization