

Decision-Making under Uncertain Conditions: The Internist, as a Director of the Diagnostic/Therapeutic Pathway in Grey Zones

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Abstract

The internists should utilize both their clinic experience and medical literature's evidences, mediating with organizational context, patients' opinion and ethics. However, none of these components may be sufficient.

In several medical sectors, we may find many and extensive grey zones in which a diagnostic intervention's effectiveness and/or its alternatives are uncertain.

This cannot lead to the decision-making process's paralysis, because the evidence-based medicine requires to base any clinical decision on "the best available evidences" and not on "the best possible evidences."

Clinicians should be able to extrapolate the prevailing question structuring from patients' problem (PICO: problem, intervention, confront, outcome); identify the best available evidence and synthesize it; perform critical evaluation and information transfer (critical appraisal); in clinical efficiency, evaluate any action options.

Keywords

Hospitalist; Internal Medicine; Clinical Error; Complexity

In general, medicine is considered as an inexact science for three main reasons:

Failure rate and uncertainty are secondary to clinical error (being it cognitive or system flaws-related: clinical risk)

Statistician William Deming showed how reduced is the acceptable failure rate in several major business sectors "If we had to tolerate living with a level of efficiency equal to 99.9 % we would have two dangerous landings a day, only in the O'Hare airport in Chicago. Every hour there would be 16.000 failed correspondence addresses, and 32.000 bank cheques withdrawn from a wrong bank account."

In comparison, medical practice exhibits a remarkable anomaly. If the error extent is underestimated, the poor understanding of its nature is alarming as well.

In a recent study, physicians attributed the main failure rate to undersized staff combined with work overload while they did not mention cognitive causes. However, several studies show that the 1/6 of medical errors occurs synthesizing available informations or deciding to act according to these [1,2].

Failure rate is inherent in diagnostic process itself, which is highly probabilistic

For example, for a proper diagnosis, diagnostic tests are not enough, because they seldom give conclusive results. Tests sensibility and specificity are inherent characteristics, which are usually provided by test manufacturers, or can be found in the literature. They determine also [3]:

a. Diagnosis variability: positive or negative predictive value is influenced by disease prevalence.

b. Biological variability of signs and symptoms' occurrence: Vital signs (blood pressure and heart rate) may vary on a daily basis and independently of other factors (position, diet, stress, physical activity etc.) In addition, many measurements, including those resulting from echocardiograms (for example, ejection fraction), are variable as well.

c. Cultural and scientific position: As to continuous measurements, such as sow blood pressure, body mass, cholesterol or glucose tolerance, which cannot be expressed by "positive-negative" dichotomy, the identification of a pathological threshold is arbitrary (as it changes with new scientific data, industrial interests, economic sustainability).

d. Complex clinic judgment: Just as happens in any other field, even in the medical area the same event can be interpreted in different ways, by different observers and at different times.

Article Information

DOI: 10.31021/ijcmc.20181101

Article Type: Case Report

Journal Type: Open Access

Volume: 1 **Issue:** 1

Manuscript ID: IJCMC-1-101

Publisher: Boffin Access Limited

Received Date: November 01, 2017

Accepted Date: December 22, 2017

Published Date: January 02, 2018

Citation: Tirotta D, Durante V. Decision-making under uncertain conditions: the internist, as a director of the diagnostic/therapeutic pathway in grey zones. Int J Clin Med Cases. 2018 Jan;1(1):101

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e. Economic elements introduction in health management: with secondary **waste** concepts (resources use, which does not change the results related to: quantity or underutilization, quality: failed exclusion despite procedures of unproven effectiveness), **saving**: less resources use (amount of resources used) and **cheapness**: proper use of resources (quality/quantity of resources used) [3,4].

Failure rate is related to lack of evidences and grey zones presence

A recent perspective article published in the New England Journal of Medicine points out that one crucial issue may be the perception? that health care is a twofold world in which interventions are either effective or ineffective, appropriate or inappropriate. Actually, there are large grey zones in which interventions are neither clearly effective nor ineffective —where benefits are unknown or uncertain and values may depend on patients' preferences and available alternatives.

Moreover, although in principle guidelines focus on "appropriateness," we should underline that appropriate care is not the same as necessary care. Many areas of medicine have recently undergone near continuous innovation process (imaging, cardiology, oncology, and orthopedics), which involved a rapid cost growth. Unfortunately, new tools "appropriate" use mostly occurs in grey zones where, although a procedure is unlikely to be harmful, its benefits may be modest or unproven [5].

As hospitalists, internists should utilize both their clinic experience and medical literature's "evidences", mediating with organizational context, patients' opinion and ethics. However, none of these components may be sufficient.

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This cannot lead to the decision-making process's paralysis, because the evidence-based medicine requires to base any clinical decision on "the best available evidences" and not on "the best possible evidences."

Clinicians should be able to:

1. Extrapolate the prevailing question structuring from patients' problem (PICO: problem, intervention, confront, outcome)
2. Identify the best available evidence and synthesize it.
3. Perform critical evaluation and information transfer (critical appraisal).
4. In clinical efficiency, evaluate any action options: internists should always wonder whether these will produce:
 - more positive than negative effects (efficacy)
 - Proper functioning in usual clinical practices circumstances (effectiveness)
 - Benefits in relation to the resources used (efficiency), and
 - Potential risks.

As an example, we will report some cases related to internists' clinical decision-making process in the grey zones.

Case 1: Therapeutic decision for a usual pathology, but with an unusual presentation

Clinical case: A 55-year-old man has come to our ultrasound outpatient department because of hematuria. Abdominal ultrasound showed two, bilateral, hypoechoic and non-homogeneous large renal masses (right: 10 cm, left: 7 cm, respectively).

Laboratory tests showed that creatinine and glomerular filtration rate were still within acceptable limits (creatinine: 1.2; glomerular filtration rate: GFR 60 ml/min).

The patient underwent tomographic evaluation of his illness along with urological assessment: the urologist gave no indications for the surgical approach, but suggested anti-tyrosine kinase therapy.

Background: The diagnosed pathology (Renal Cell Carcinoma: RCC bilateral synchronous) is quite unusual.

Do we have necessary evidences for a therapeutic procedure? Is the decision not to perform surgery secondary to cognitive bias (diagnostic-therapeutic inertia/ omission bias)?

Clinical problem (PICO): In a patient with massive renal synchronous neoplasia (RCC), is medical therapy, compared to surgical therapy, the only way to improve survival?

Best available evidence identification: Nephrectomy is usually recommended as a first step in RCC. However, since the observed pathology (massive renal synchronous neoplasia) is unusual, routinary recommendations cannot apply. Medline Literature's extensive research features only observational studies, retrospective and international registers. It emerges that the extent of the disease has no significant influence on the decision to perform surgery. Patients with estimated survival time equal to < 12 mo or 4 further IMDC (International Metastatic Renal Cell Carcinoma Database Consortium) prognostic factors may not benefit from nephrectomy whereas all other patients do [6-8].

Internist - Patient communication: After being informed on risks (especially, the probable, imminent necessity for a dialysis approach) and benefits (complete mass removal), the patient opted for a radical surgery approach.

Evolution: Considering patient's young age, good performance status, medical history and will, the internist asked for a second opinion in another Medical Center with a high number of relevant clinical cases (as recommended in case of unusual diseases), where the man underwent radical (right side) and partial (left side) nephrectomy. One year later, he is still asymptomatic with good GFR.

Case 2: Diagnostic – Therapeutic decisions related to unusual pathology

Clinical case: In the last months, a 60-year-old woman has experienced progressive asthenia, fever and paraplegia due to a voluminous retroperitoneal, paravertebral mass which was difficult to get access to, confirmed by abdominal tomography (TC).

We performed a guided TC biopsy (repeated twice because of initially insufficient evidences) that showed a suspicious lymphoma with two components:

- low kinetic phenotype index with germinal center.
- T-cells with high proliferative index/large cell B.

The slides were examined also in another reference center, where they confirmed the apparent double population, although histological report was lacking Negative osteomodulatory biopsy.

Clinical problem (PICO): In a patient with a probable composite lymphoma, has a histological characterization the greatest impact on survival, even with diagnostic latency increase, or is a therapy tout court more appropriate, considering the available histology?

Background: A composite lymphoma consists of two or more different morphological types of malignant lymphoma affecting the same organ or tissue. Most of the reported cases show a combination of classic Hodgkin lymphoma with B-cell lymphoma. The co-occurrence of B and T cell lymphoma, however, is a rare event. Does therapeutic latency, justified by hardly-obtained detailed diagnostics, worsen the prognosis only?

Best available evidence identification: Only case reports with aggressive course are reported. In response cases, a correct histological characterization is crucial to ensure greater therapeutic appropriateness [9-16].

Internist - patient communication: We talked to the patient and his family, pointing out the difficulties her diagnosis involved, due both to the mass location, and disease severity. We considered to adopt a diagnostic surgical approach, although difficult to implement. She asked to be moved to another Hematology department where she started the therapy.

Evolution: The patient started the therapy for lymphoma B with high proliferative index. The evolution was unfavourable. Even so, following a meeting, a decision was taken by common agreement between the internist, the hematologist colleagues, the patient and her family. Unfortunately, the patient died 5 months later.

Case 3: Diagnostic and therapeutic decision related to a non-recurring pathology, with confounding bias

Clinical Case: Two years ago, a 55-year-old-man came to our outpatient department with a chronic hepatitis B and hepatic injury, which was interpreted as an angioma. His medical history was negative, especially for alcohol/smoke abuse. Liver tests were normal. He underwent US abdomen positive for multiple liver hyperechoic nodules, attributed to hemangiomas, but of uncertain nature, with abdomen CT/MRI performed 3 months before. FPDG PET was negative.

Clinical problem (PICO): In a patient with chronic hepatitis B, should the presence of hepatic hyperechoic lesions be further investigated for a better diagnostic outcome?

Background: Patients affected by rare diseases find it hard to obtain good quality healthcare, due, among the others, to lack of scientific and multidisciplinary healthcare knowledge as well as to diagnostic delays. Cognitive bias accounts for late diagnosis and ineffective therapeutic path, especially in the case of rare diseases such as NET (neuroendocrine tumor), a long-unrecognized disease (just like 90% of NET).

Internists' role is to analytically reason on this diagnosis, and introduce the patient to a multidisciplinary path.

Best available evidence identification: The guidelines suggest that any injury in an unhealthy liver should be further investigated with the highest possible level of evidence. The confounding bias here was the exclusion of the most common pathologies, for the expectation phenomenon (Ascertainment bias) [17-19].

Evolution: We performed CEUS (suggestive of metastases) and liver biopsy, positive for NET metastases (GRAD1, Ki67 2%).

However, according to the most recent NET guidelines, after discussing with the patient and the NET Reference Centre, we performed Ga68DOTANOC PET, positive for focal hypermetabolic area in terminal ileum, mesenteric adenopathy, pericardic and multiple liver nodules [18-19].

The patient started the therapy including Sandostatin LAR (1 for every 28 days) and octreotide (0.1 x 2 for 7 days) and underwent ileal resection and cholecystectomy.

After 3 months' therapy he underwent radiometabolic therapy and now, after one year, he is in good clinical conditions.

Clinical reasoning should allow for the inclusion of an unusual pathology and should organize a multidisciplinary path.

Conclusion

Appropriateness is commonly understood as "the level of assistance really necessary to the patient, for so it can become appropriate to the best and newest available scientific evidences."

Any "appropriate" decision complies with the six right things' rule: the right medication, for the right individual, in the right moment, from a right professional, in the right dose, with the right documentation. Actions' quality needs to be considered in relation both to objectives and execution mode [20].

From the examined cases we clearly infer that medicine is a complex system. The internists' cultural background can be a helpful guide in grey zones and beyond, by mediating six fundamental points of view: the patient, the doctor, the evidences, the non-evidences, the organizational/social/economic context and the inter professional cooperation (Figure 1).

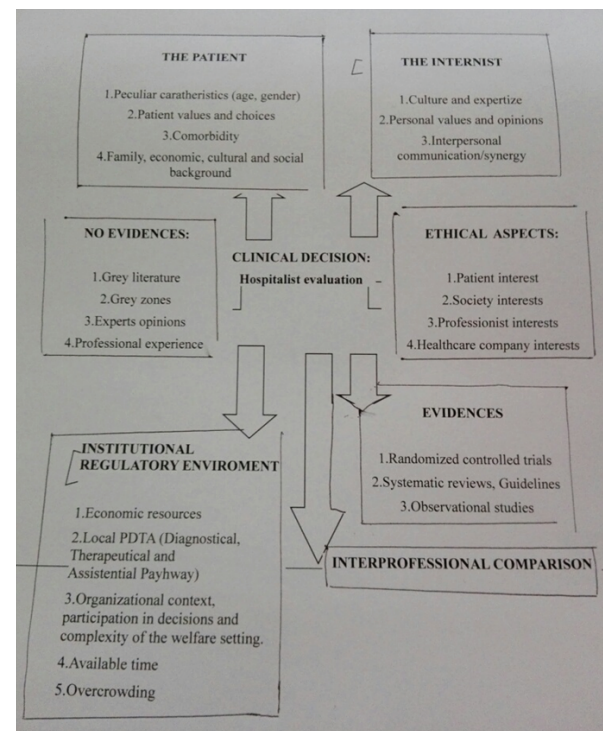


Figure 1: Complexity of medicine and role of the internist

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