Critically Appraised Topics

Topic: **Benefits of Anti-hypertensive Therapy for the Elderly**

Reviewer: Jeffrey Chua, MD

Clinical Scenario: An 82 year old female family friend is consulting you regarding her blood pressure. Having been on a calcium channel blocker for a year, her daily blood pressure ranges from 160-170/90 mmHg. She is asymptomatic, has no other illnesses, maintains a relatively healthy active lifestyle and does not smoke. Her recent ECG and 2D echo reports were essentially normal. She is wary regarding lowering her blood pressure since she read that BP reductions in her age group to normal levels did not translate to reduction in mortality. However, she expresses her concern regarding the risk of heart failure and stroke if she did not reduce her blood pressure.

Clinical Question: Among hypertensive patients aged 80 years or older, how effective is anti-hypertensive therapy in reducing the risk of stroke, heart failure, and death from cardiovascular and any cause?

Citation: Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D et al for the HYVET Study Group. Treatment of Hypertension in Patients 80 Years of Age or Older. N Engl J Med. 2008; 358: 1887-98.

Appraising Directness

Does the study provide a direct enough answer to your clinical question? **YES**

Population: Hypertensive patients aged 80 years or older

Intervention: Indapamide (sustained release, 1.5mg) vs. Placebo with or without Perindopril (2mg or 4mg)

Outcome: Reduction in the risk of fatal or non-fatal stroke, death from any cause, death from cardiovascular causes, death from cardiac causes, and death from stroke.

Appraising Validity

Randomized?	YES
Allocation concealed?	YES
Baseline characteristics similar?	YES
Blinding of subjects?	YES
Blinding of caregivers?	YES
Blinding of outcome assessors?	YES
Intention-to-treat analysis?	YES
Drop-out not significant?	YES

Interpreting Results

Outcome	Rc	Rt	RRR	ARR	RR	NTT	Hazard Ratio
Stroke	3.6%	2.6%	28%	1%	0.72	100	0.70
Death from stroke	2.2%	1.4%	36%	0.8%	0.64	125	0.61
Death from any cause	12.3%	10.1%	18%	2.2%	0.82	45	0.79
Death from CV cause	6.3%	5.1%	19%	1.2%	0.81	83	0.77
CHF	3%	1.1%	63%	1.9%	0.37	53	0.36

Assessing Applicability:

Biological Issues: The results can be applied to our patient, since her characteristics fit with the characteristics of the patients included in the study. The study included almost 40% coming from Asia and the other majority coming from Europe. The question regarding the effectiveness of the study intervention based on racial differences can be disregarded. In totality, the results of this journal article can be applied to our patient's case.

Socioeconomic Issues: None

Individualizing Results

Patient's baseline risk for developing major cardiovascular event as well as risk factors for an adverse outcome is comparable to that of the study population. Based on the NNTs, if we treat 200 patients with Indapamide SR 1.5 mg (P25/tab), Indapamide 1.5 mg + Perindopril 2 mg (P39/tab), and Indapamide 1.5 mg + Perindopril 4 mg (P48/tab) daily for 1 year to achieve a target blood pressure of 150/80 mmHg, overall expense would be P1,825,000.00, P2,847,000.00, and P3,504,000, respectively, and this amount of money spent could prevent 2 strokes, 2 deaths from stroke, 5 deaths from any cause, 3 deaths from cardiovascular cause, and 4 CHF. Adverse effects such as hypokalemia, hyperglycemia, and azotemia may occur negligibly, which in the study showed no significant difference among the patients in both treatment groups in the mean baseline changes from baseline in the serum potassium, glucose and creatinine, respectively. Given the high cost of treatment but negligible adverse effects, the patient will be more likely to benefit from the treatment.

Author's Conclusion

The results provide evidence that antihypertensive treatment with indapamide (sustained release), with or without perindopril, in persons 80 years of age or older is beneficial.

Bottomline...

Treatment with Indapamide (sustained release), with or without Perindopril, in persons aged 80 years or older is beneficial in terms of reducing risk of stroke, CHF, and death, with minimal adverse effects. The cost of treatment will still have to be considered.

Reference:

Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D et al for the HYVET Study Group. Treatment of Hypertension in Patients 80 Years of Age or Older. N Engl J Med. 2008; 358: 1887-98.

Topic: **Utility of NT Pro BNP in Diagnosis Structural Heart Disease among Patients with Atrial Fibrillation**

Reviewer: Helenne Joie Brown, MD

Clinical Scenario: A general practitioner friend of yours is concerned about requesting a 2DED for one of his financially challenged patients who complains of easy fatigability and has borderline cardiomegaly on chest x-ray and atrial fibrillation in ECG. He asks you if there is any blood test that could help verify the presence of structural heart disease. Being a fellow-in-training in cardiology, you ask one of your mentors who suggested the use of NT pro-BNP. Your friend requested the test and the result was elevated at 1000 pg/ml. However, on further reading, you note that NT-pro-BNP may be increased in cases of atrial fibrillation. You wonder then if this test can be applicable to your friend's patient after all.

Clinical Question: Among patients with cardiac dysrhythmia, how well can NT pro-BNP diagnose structural heart disease?

Citation: Shelton RJ, Clark AL, Goode. Rigby A, and Cleland JGF. The Diagnostic utility of N-terminal pro-B-type natriuretic peptide for the detection of major structural heart disease in patients with atrial fibrillation Eur Heart J. 2006;27, 2353-2361.

Appraising Directness

Does the study provide a direct enough answer to your clinical question? **YES**

Population: Patients with atrial fibrillation

Intervention: N-terminal pro-Brain natriuretic peptide

Outcome: structural heart disease

Appraising Validity

Reference standard	
Acceptable?	YES
Interepreted independently from test question?	YES

Interpreting Results

NT pro BNP (pg/ml)	Sn (%)	Sp (%)	PPV (%)	NPV (%)	(+) LR (%)	(-) LR (%)
1000	90	50	83	65	1.8	0.20

In our clinical scenario, the level of NT pro-BNP was 1000 pg/ml. At this level, in detecting structural heart disease in patients with AF, the sensitivity of NT pro-BNP is 90 %, specificity 50%, positive predictive value 83%, negative predictive value 65%. The likelihood ratio is 1.8; thus there is a 1.8-fold increase in the odds of disease (i.e. structural heart disease) in patients with AF given an NT-pro-BNP reset of 1000 pg/ml.

Assessing Applicability:

Biological Issues:The results can be applied to our clinical setting. The population included patients, both in sinus rhythm as well as in atrial fibrillation, aged 69 years and above, including both males and females in almost equal number. There was no mention of the race of the study participants. Co-morbid conditions included ischemic heart disease, hypertension, diabetes and cerebrovascular disease. However, the diagnostic utility of the test is affected by the age of the patient and the cardiac rhythm whether atrial fibrillation or sinus rhythm.

Socioeconomic Issues: NT-pro-BNP is an expensive diagnostic test which is available only in a few centers in Metro Manila, presently unavailable at the Philippine Heart Center.

Individualizing Results

The patient in our clinical scenario has an NT-proBNP level of 1000 pg/ml. Using the Fagan's nomogram, if I set the pretest probability at 90% and plot it with a likelihood ratio of 1.8, then the post-test probability of structural heart disease is 90%.

NT-pro-BNP is not available in all hospitals. Its present cost is P3,650. Compared with a 2DED which was used as a reference standard in this trial, the price of the 2 tests are comparable. We should thus inform our patient and let him/her make an informed choice about which diagnostic test to be performed.

Author's Conclusion

Atrial fibrillation causes an elevation of NT-proBNP in patients without major structural heart disease and across the entire spectrum of such disease. If NT-pro BNP is to be used as a screening tool in patients with AF, significant adjustments to current proposed cut-off values are required to maintain its diagnostic utility.

Bottomline...

NT-pro-BNP at higher values, i.e > 1000 pg/ml has diagnostic utility for structural heart disease in patients with atrial fibrillation.

Reference:

Shelton RJ, Clark AL, Goode. Rigby A and Cleland JGF. The Diagnostic utility of N-terminal pro-B-type natriuretic peptide for the detection of major structural heart disease in patients with atrial fibrillation Eur Heart J. 2006; 27, 2353-2361.

Editor's Note:

CATs are critical appraisal of a journal article that addresses a clinical question. Clinical questions are often encountered during patient encounters, reading articles and conferences. Given the flux of medical information available, CATs can be considered as tools that can be use by a busy clinician or a trainee or an academician to select articles applicable to their clinical question. In doing CATs, we assess the directness, validity and applicability of an article; interpret and individualize the results; and arrive at a reviewer's conclusion or clinical bottomline.

The reviewers of CATs published here are fellows-in-training. They were given workshops in doing CATs and they have been practicing doing CATs as part of their training. The appraisal of the articles are made by them and statements and opinions expressed by them do not necessarily reflect those of the editors and publishers.