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Lately accreditation labels have become unique selling propositions (USPs) for corporate and private sector hospitals. The certification is flaunted with gay abandon to attract patients and claim superiority over contemporaries. In fact encashing on the embedded Indian psyche and mentality favouring anything foreign, corporate hospitals have gone beyond their means to seek the accreditation of the Joint Commission International (JCI) of United States of America (USA). The moot question however is whether the accreditation process helps improve outcomes and deliver better care for the patients?

If a recent study from Brigham and Women’s Hospital and the Harvard TH Chan School of Public Health, Boston is to be believed, then the answer is a clear ‘No’.1 When Lam et al. compared patient outcomes in form of mortality, 30 day readmission or improved patient experience, they found no difference between hospitals accredited by Joint Commission as opposed to those reviewed by a state accreditation body.1 In fact surprisingly patient experience scores were numerically better at hospitals accredited by state agencies (3.4 versus 3.2; P - 0.06). This assumes significance when seen in the light of the fact that these accreditation processes are both time and labour intensive, besides being prohibitively costly. It is estimated that the commission fees for an inspection was US dollar 18,000 in 2015 on top of an annual fee of up to US dollar 37,000.

A lot of times additional manpower mandated by these inspections, as also the infrastructural changes, are not practically relevant and add to wasteful and frivolous expenditure for a hospital, which no doubt is ultimately passed on to the patient in one form or the other. This becomes all the more relevant for a developing and poor country like India where patients have to spend upwards of 85% of medical expenses out of their own pockets. The western benchmarks are not relevant to India but unfortunately Indian accreditation agencies like NABH and NABL have adopted a lot of those parameters without sparing a thought on their relevance to Indian scenario. Even the infrastructural requirements mandated by commissions like Joint Commission Internationa of USA are impossible to meet in Indian scenario.

Thus just as when we talk of cost containment, the accreditation mania leads to escalation of costs, sans any meaningful advantage in hard endpoints of patient outcomes. To meet the complex requirements of these accrediting bodies and to understand and decipher the various jargons used by them, most hospitals employ...
a professional agency to help them sail through this rather arduous journey, thereby surreptitiously contributing to a multi-million dollar bustling and thriving industry.

It’s therefore time that we have a good relook at the need and the content of the accreditation process and lay down the minimum criteria, keeping the ground realities in mind. The extra fiscal resources allocated to accreditation can only be justified if these translate into improved patient outcomes which are measurable, verifiable and reproducible.

REFERENCE
Hypertension Case Study

PEEYUSH JAIN, ASHOK SETH

Abstract
Hypertension is a common problem in the elderly population. In this case report, the 76-year-old patient is having uncontrolled hypertension, diabetes, and renal dysfunction. Previously patient was treated with atenolol, amlodipine, and indapamide sustained release for the past three years. But blood pressure (BP) is varying between 156-168/76-88 mmHg. For such patients home blood pressure monitoring is advisable and desirable control on BP is required to minimize the cardiovascular complications. Overall, controlling the BP is art and science which need right medication, doses, timing, and lifestyle modifications.

CASE
A 76 years old patient with diabetes mellitus and hypertension receiving atenolol, amlodipine, and indapamide sustained release for last 3 years has been referred for further BP management. In GP’s clinic, BP is found to vary between 156-168/76-88 mmHg. In hospital OPD, BP is 174/96 mmHg, checked twice. Hb 10.5 g/dl, BU 52 mg/dl, Serum Creatinine 1.6 mg/dl, Serum Na+ 138 mmol/L, K+ 3.4 mmol/L. Patient is advised home blood pressure monitoring (HBPM). Two weeks later self-monitored BP 140-146/72-84 mmHg (morning) and 154-172/68-96 mmHg (evening).

DISCUSSION
This patient is at very high-risk of future cardiovascular events because of age, uncontrolled hypertension, diabetes mellitus, and renal dysfunction (Table 1, ESH/ESC 2018 Guidelines for Hypertension Management). Therefore his blood pressure needs to be controlled meticulously.

The first step in effective blood pressure management is accurate measurement of blood pressure. While this a diagnosed case of hypertension, misdiagnosis of hypertension is very frequent and due to several biological and patient, environment, equipment, and method-related factors (Table 2).

Methodological issues apart, a recent confounding factor of major importance is varying definitions of hypertension suggested by different...
hypertension organizations and even by same organization within a short span of time (Table 3). This is an issue that can be discussed at length without consensus but there are some arguments against lowering of diagnostic threshold of hypertension to 130/80 mmHg (Table 4).

Let us say for the purposes of this discussion that a more suitable diagnostic threshold for hypertension is 140/90 mmHg. So what are his BP targets? European guidelines suggest a BP target for such a patient as 130-139/70-79 mmHg (Table 5).

An important consideration at this point is the choice of antihypertensive drug therapy. It is prudent to optimize antihypertensive medication and try to achieve office BP target by the end of next one month or so. Both atenolol and amlodipine do not seem to be the best choice in this patient. Limitations of atenolol are its low efficacy, poor excretion in presence of low GFR and propensity to aggravate glucose intolerance. A better choice is an ACE-I/ARB and if there is a compelling indication for beta blocker, carvedilol due to its vasodilating property. Amlodipine is limited by theoretical possibility to raise intra-glomerular pressure due to selective dilatation of afferent arterioles and may be substituted by benidipine or cilnidipine both of which dilate afferent as well as efferent arterioles. Mild hypokalemia due to indapamide in this patient may be counteracted by addition of ACE-I/ARB, potassium rich diet, or MRA if this patient proves to be resistant in future. Substituting chlorthalidone or other thiazide diuretic does for indapamide does not seem to be desirable as these may be cause even more intensive hypokalemia (Table 6).

Let us assume that office blood pressure has been reasonably controlled by above changes in medication. This may take at least a month or may be more. But there are other issues related to blood pressure that need further attention. One of the foremost is whether controlling office blood pressure is enough. Several studies have shown that blood pressure control improves with HBPM. Secondly, 4 out of 5 studies that compared HBPM with office BP concluded that HPB is a better predictor of cardiovascular

Table 1: Cardiovascular Risk Assessment in Hypertension

<table>
<thead>
<tr>
<th>Blood Pressure (mmHg)</th>
<th>No other renal failure</th>
<th>1-2 renal failure</th>
<th>&gt;3 renal failure</th>
<th>OD, CKD Stage 3 or Diabetes</th>
<th>Symptomatic CVD, CKD Stage &gt;4 or DM with OD/renal failures</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Normal (130-139/85-89)</td>
<td>Low Risk</td>
<td>Moderate Risk</td>
<td>High Risk</td>
<td>Moderate to High Risk</td>
<td>Very High Risk</td>
</tr>
<tr>
<td>Grade 1 (140-159/90-99)</td>
<td>Moderate Risk</td>
<td>Moderate-High Risk</td>
<td>High Risk</td>
<td>High Risk</td>
<td>Very High Risk</td>
</tr>
<tr>
<td>Grade 2 (160-179/100-109)</td>
<td>High Risk</td>
<td>High Risk</td>
<td>High Risk</td>
<td>High-Very High Risk</td>
<td>Very High Risk</td>
</tr>
<tr>
<td>Grade 3 (&gt;180/110)</td>
<td>High Risk</td>
<td>High Risk</td>
<td>High Risk</td>
<td>High-Very High Risk</td>
<td>Very High Risk</td>
</tr>
</tbody>
</table>

Table 2: Pitfalls in measurement and interpretation of blood pressure

<table>
<thead>
<tr>
<th>Example (s)</th>
<th>Biological phenomenon-related</th>
<th>Patient-related</th>
<th>Environment-related</th>
<th>Equipment related</th>
<th>Method-related</th>
<th>Personnel-related</th>
<th>Interpretation-related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regression to the mean</td>
<td>Sleep deprived</td>
<td>Cold ambient temperature</td>
<td>Non-calibrated</td>
<td>Fast bleed rate</td>
<td>Terminal digital preference</td>
<td>Definition of hypertension</td>
<td></td>
</tr>
<tr>
<td>Air leaks</td>
<td>Missing auscultatory gap</td>
<td>DBP Phase IV or V?</td>
<td>Single reading</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Definition of Hypertension: European or American Guidelines

<table>
<thead>
<tr>
<th>Blood Pressure (mmHg)</th>
<th>ESH/ESC 2018</th>
<th>AHA/ACC 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>≥140 and/or</td>
<td>≥130 and/or</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>≥90</td>
<td>≥80</td>
</tr>
<tr>
<td>ABPM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24h Average</td>
<td>≥130 and/or</td>
<td>≥125 and/or</td>
</tr>
<tr>
<td>Day Average</td>
<td>≥135 and/or</td>
<td>≥130 and/or</td>
</tr>
<tr>
<td>Night Average</td>
<td>≥120 and/or</td>
<td>≥110 and/or</td>
</tr>
<tr>
<td>HBPM</td>
<td>≥135 and/or</td>
<td>≥130 and/or</td>
</tr>
<tr>
<td></td>
<td>≥85</td>
<td>≥80</td>
</tr>
</tbody>
</table>

Table 4: Some arguments against lowering of diagnostic threshold for hypertension to 130/80 mmHg

- It has huge public health implications.
- A considerable number of low-risk people shall be treated pharmacologically without benefit.
- At times it is not possible to reduce blood pressure to such low levels without unacceptable side effects.
- In some cases, systolic blood pressure cannot be reduced below 140 mmHg without marked fall in diastolic blood pressure. This is particularly true of elderly with isolated systolic hypertension.
outcomes. HBPM is also helpful in making a diagnosis of white coat hypertension and masked hypertension that is not so relevant in this case. HBPM is particularly useful in elderly and pregnant or CKD patients (Table 7).

For making clinical decisions on the basis of HBPM, the patient should be advised to take ≥ 2 morning readings before medication and 2 evening readings at bedtime every day for 1 week prior to next hospital visit. Discarding the readings of the first day gives a total of 12 readings on which to make clinical decisions. For self-monitoring, patients should take at least two, preferably three readings, and record them all. The interval between can be as little as a minute. Patients need to be educated about the variability of readings. It is important to remember that home blood pressure readings are generally lower than office BP readings and that changes the definition of hypertension and treatment targets also.

For HBPM, fully automated monitors that use the brachial artery for measurements are the most reliable. Documentation can be improved if patients use monitors capable of printing and storing readings. Patient’s monitor should be checked against mercury sphygmomanometer. Oscillometric devices may not work well with patients who have atrial fibrillation or other arrhythmias. An up-to-date list of validated monitors can be found at: www.bhsoc.org/blood_pressure_list.stm (British Hypertension Society)3 or www.dableducational.org.sphygmomanometers_2_sbpm.htm#armtable (Dabl Education Trust).4

One major limitation of HBPM is that it is unable to take into account nighttime blood pressure changes (Table 8). Therefore it is unable to estimate true overall 24 hour BP and its circadian variation. Ambulatory blood pressure (ABPM) circumvents these problems and complements the information provided by HBPM (Table 9). It is also able to define effective duration of action of antihypertensive drug(s) objectively.

Ambulatory BP monitoring has revealed that blood pressure changes during sleep differ from person to person.

---

**Table 5: Office BP Targets**

<table>
<thead>
<tr>
<th></th>
<th>ESH/ESC 2018</th>
<th>AHA/ACC 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age year</td>
<td>HTN +DM +Stroke +CAD +CKD</td>
<td>SBP</td>
</tr>
<tr>
<td>18-65</td>
<td>120-130 if tolerated</td>
<td>130-139</td>
</tr>
<tr>
<td>65-79</td>
<td>130-139 if tolerated</td>
<td></td>
</tr>
<tr>
<td>&gt;80</td>
<td>130-139 if tolerated</td>
<td></td>
</tr>
</tbody>
</table>

**Table 7: Populations in Whom Home BP Measurement is Specially Useful**

<table>
<thead>
<tr>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
</tbody>
</table>

**Table 6: Choosing Antihypertensive Agents in Elderly Diabetes with CKD**

<table>
<thead>
<tr>
<th>Current Treatment</th>
<th>Limitations</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>Low Efficacy, Poor Excretion due to low eGFR, Propensity to aggravate glucose intolerance</td>
<td>ACE-I/ARB or Carvedilol</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>Intra-glomerular hypertension → Proteinuria and renal dysfunction</td>
<td>Benidipine, Cilnidipine</td>
</tr>
<tr>
<td>Indapamide</td>
<td>Mild hypokalemia</td>
<td>None, K+ rich diet, +ACE-I/ARB, +MRA if resistant</td>
</tr>
</tbody>
</table>

Abbreviations: ABPM; Ambulatory blood pressure monitoring, HBPM; Home blood pressure monitoring.

**Table 8 Comparison of 3 Main Methods of BP Measurement**

<table>
<thead>
<tr>
<th>Feature</th>
<th>OPB</th>
<th>ABPM</th>
<th>HBPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Readings</td>
<td>Low</td>
<td>High</td>
<td>Medium</td>
</tr>
<tr>
<td>White Coat Effect</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Operator Dependency</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Night-time BP</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Early Morning BP</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>24 h Variability</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Long-term BP Variability</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>WCH and MH Diagnosis</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Reproducibility</td>
<td>Low</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Prognostic Value</td>
<td>+</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Hypertension Control Improvement</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
</tbody>
</table>

Abbreviations: WCH; white coat hypertension, MH; Masked hypertension.

**Table 9: Indications of Ambulatory BP Monitoring**

<table>
<thead>
<tr>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>To make a diagnosis of hypertension (major indication)</td>
</tr>
<tr>
<td>To rule out borderline hypertension with end-organ damage</td>
</tr>
<tr>
<td>To investigate labile/paroxysmal hypertension</td>
</tr>
<tr>
<td>To evaluate symptoms possibly related to BP fluctuations, especially orthostasis</td>
</tr>
<tr>
<td>To evaluate orthostatic hypotension, autonomic neuropathy, and carotid sinus syncope</td>
</tr>
<tr>
<td>To assess adequacy of antihypertensive therapy</td>
</tr>
</tbody>
</table>
who exhibit extreme fall in nocturnal blood pressure. (Table 10). Addressing these issues at therapeutic level require changes in the choice, doses, and timings of antihypertensive agents but this is largely an art based on a sound knowledge of the pharmacokinetics of antihypertensive drugs. Some practical considerations related to ABPM are summarized in Table 11-13.

**SUMMARY**

This is a high-risk patient in whom a good control of BP is highly desirable to reduce cardiovascular and renal risk. Two minimum requirements in this patient are (i) right-choice of antihypertensive medication combination and (ii) achievement of office BP targets. Control of office BP alone is not adequate. Minimizing BP burden will require (i) HBPM and its interpretation (ii) adjusting medication choice, dose and timing for night-time and early morning variations in BP. Here, ABPM should help. ABPM may precede HBPM or vice versa. While HBPM may be performed as many times as necessary, ABPM is limited due to cost and convenience. Treatment of high blood pressure is both a science as well as an art. It requires setting reasonable targets, choosing the right medication, doses, and schedules, and monitoring beyond office BP measurement.

**REFERENCES**

3. www.bhsoc.org/blood_pressure_list.htm
4. www.cableducational.org.sphygmomanometers_2_sbp.htm#armtable

**Table 10: Dipping Status**

<table>
<thead>
<tr>
<th>Dipping Status</th>
<th>Daytime vs. Nighttime Average</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipper</td>
<td>10-20% dipping</td>
<td>Normal</td>
</tr>
<tr>
<td>Non-dipper</td>
<td>&lt;10% dipping</td>
<td>Increased BP burden</td>
</tr>
<tr>
<td>Reverse dipper</td>
<td>Rise in BP at night</td>
<td>Increased BP burden</td>
</tr>
<tr>
<td>Extreme dipper</td>
<td>&gt;20% dipping</td>
<td>Cognitive impairment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anterior ischaemic optic atrophy</td>
</tr>
</tbody>
</table>

**Table 11: Contraindications/Barriers to ABPM**

- Not cooperative/Unwilling
- Severe office hypertension (≈220/120)
- Arm too big (above 48-50 cm)
- Severe peripheral vascular disease or thrombocytopenia

**Table 12: Practical Considerations in ABPM**

- Use a proper sized cuff.
- Use the non-dominant arm unless the dominant arm has 10 mmHg or greater BP.
- Test an initial reading to be sure it’s working.
- Have the patient keep a diary.
- Adjust the settings to correspond to bedtime and time awake.
- Ask them to stop and stand still when a reading is being taken if possible.
- Go about their daily routine but ask them not to exercise.

**Table 13: Office vs. HBP and ABP**

<table>
<thead>
<tr>
<th>Clinic</th>
<th>HBPM</th>
<th>Daytime ABPM</th>
<th>Nighttime ABPM</th>
<th>24-hour ABPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>120/80</td>
<td>120/80</td>
<td>120/80</td>
<td>100/65</td>
<td>115/75</td>
</tr>
<tr>
<td>130/80</td>
<td>130/80</td>
<td>130/80</td>
<td>110/65</td>
<td>125/75</td>
</tr>
<tr>
<td>140/90</td>
<td>135/85</td>
<td>135/85</td>
<td>120/70</td>
<td>130/80</td>
</tr>
<tr>
<td>160/100</td>
<td>145/90</td>
<td>145/90</td>
<td>140/85</td>
<td>145/90</td>
</tr>
</tbody>
</table>

Normally there should be 10%-20% decrease from daytime BP during sleep. Both non-dipper and reverse dippers carry excessive blood pressure burden. Measures should be taken to reverse these trends to improve clinical outcomes. At the other end of the spectrum are those who exhibit extreme fall in nocturnal blood pressure. (Table 10). Addressing these issues at therapeutic level require changes in the choice, doses, and timings of antihypertensive agents but this is largely an art based on a sound knowledge of the pharmacokinetics of antihypertensive drugs. Some practical considerations related to ABPM are summarized in Table 11-13.
Echocardiographic Evaluation of Prosthetic Heart Valve; special reference to TEE and 3D echo

ASHOK K OMAR, RAHUL KUMAR

Abstract
In the last five decades multiple different models of prosthetic valves have been developed. The purpose of this article is to provide a comprehensive source of information for the types and the echocardiographic evaluation of the prosthetic heart valves.

INTRODUCTION
First successful artificial heart valve was implanted in year 1960. The evaluation of prosthetic heart valves remained a challenge since their utilization for five decades. This is partly due to different variety of prosthetic heart valves (PHV) and their unique features. Worsened condition of PHV patients is not always due to dysfunction of PHVs, instead it may be due to progressive left or right ventricular failure, arrhythmias, pulmonary hypertension etc. These conditions and acoustic shadows and artefacts during echocardiography made heart valves evaluation one of the difficult subject for echocardiography. Science is evolving from the beginning, we are having newer and advanced techniques for PHVs evaluation.

Among PHVs, almost all are obstructive in nature due to their own structure and it is difficult to differentiate it from pathological obstruction. Trivial or mild regurgitation through the valves is usually present which is normal but the pattern differs among the different types of valves. Although PHV dysfunction is rare but it may be potentially life threatening. Thus, it is very essential to establish the exact cause of PHV dysfunction so as to plan the appropriate management of the patient. To detect the cause and extent of PHV dysfunction, a comprehensive approach which integrates different parameters of morphology and function assessed by 2D TTE (Transthoracic Echocardiogram), TEE (Transesophageal echocardiogram) and 3D echocardiography is mandatory. Other
tools for diagnosing PHV dysfunction are cinefluoroscopy, multidetector CT, cardiac magnetic resonance imaging (CMR) and nuclear imaging.

Although the first-line imaging of PHV evaluation is 2D TTE. However due to shadowing and reverberation artifacts, a complete assessment cannot be done without adding TEE, which allows more detailed assessment about cusps calcification, vegetations, thrombus, pannus and leaflet mobility. Absence of interference with lungs and ribs make TEE a good choice for PHV evaluation. A very detailed image can be obtained of the atrial side of mitral PHV and of the posterior part of the aortic PHV. Anterior part of the aortic prosthesis is often obscured by acoustic shadowing from the prosthetic material and is often better seen by TTE.

Earlier techniques to reconstruct 3D images enabled improved visualization of valvular anatomy but acquisition of images was tedious, time consuming and more post-process requiring. The image quality was also poor and frequently affected by artifacts which limited its use for research purpose. Whereas the recent advances in real-time 3D (RT3D) TEE have launched this technique into clinical practice. Matrix array (more than 3000 elements) has enabled TEE probe real time acquisition and on line display of 3D TEE images. RT3D TEE has allowed improved visualization and assessment of prosthetic valves.

**TYPES OF PROSTHETIC HEART VALVES**

PHVs are either biological or mechanical. Most frequently implanted biological PHVs are stented xenografts which are made of bovine pericardium or from pig aortic valve. Stentless prosthetic valves were introduced to improve hemodynamic durability and reducing complications. Stentless bioprosthetic valves usually consist of preparation of porcine aorta, may be little long or may be made to fit under coronary arteries. Some are made from bovine pericardium. Table 1, Figure 1.

Homografts (Allografts) are stentless and consist of human aortic or sometimes pulmonary valve which are cryopreserved. They have good durability if harvested early after death and do not need anticoagulation. For this reason they may be used as an alternative to mechanical PHV in young individuals. Homografts resist infection and can be used in patients of infective endocarditis. Ross procedure is substituting the patient’s diseased aortic valve by his own pulmonary valve. Along with, a homograft is implanted in pulmonary position. It has a good durability and it may grow in children and less prone to infection than xenograft. Sutureless valves were developed for implantation and reducing the bypass time. Recent development is transcatheter valves for the patients having high or intermediate risk for conventional valve replacement. The most commonly implanted are Edward Sapien-a balloon expandable valve or Medtronic Core valve. Newer generation of these valves are introduced to reduce the complication related to implantation of these valves. Some new designs like Jena valve can be utilized in native aortic regurgitation. Transcatheter valves are increasingly used inside failed stented aortic and mitral replacement.

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**Figure 1: Types of prosthetic heart valves**
Biologic Stentless Self-expandable Percutaneous

Immediately between 3-12 weeks

ECHOCARDIOGRAPHY FOR PHV

GUIDELINES FOR ECHOCARDIOGRAPHY FOR PHV

- Immediately between 3-12 weeks after valve replacement surgery, to confirm normal function and to establish a hemodynamic marker. Routine echo after this is not indicated for mechanical valves because their risk of primary failure is almost nil.

- If age of the patient is < 50 years, then for biological valves routine echocardiographic evaluation to detect any structural degeneration or any dysfunction should be performed at five years, but when the age of the patient is more than 50 years the same should be performed at ten years. The biological valve failure rate is 20% in aortic position and 40% in mitral position is 10 years.

- If there is presence of new murmur or any symptom of valvular dysfunction, echocardiographic evaluation PHVs should be performed.

- Presence of clinical evidence of infective endocarditis.

- If any major noncardiac surgery is planned.

- Before conceiving and during pregnancy in each trimester.

- When a patient presents with abnormal signs and symptoms and he is a PHV recipient, we should also exclude the ventricular dysfunction (LV or RV). Other valvular dysfunction and cardiac tamponade, besides evaluation of the PHV dysfunction.

- If any symptom of valvular dysfunction, echocardiographic evaluation to detect any structural degeneration or any dysfunction should be performed.

- Routine echo after this is not indicated for mechanical valves because their risk of primary failure is almost nil.

- First-line imaging for PHV evaluation is 2 D TTE, should be added for complete evaluation of PHV. The complete echocardiographic imaging of the PHV includes multiple views like parasternal long axis, parasternal short axis, apical 4 chamber view and some off axis views (Figure 2).

- Multiple angulation of the probe is required for full TTE evaluation. Rarely, intermittent obstruction is suspected, in that case prolonged Doppler examination is utilized. Often TTE is not adequate and TEE is needed for PHV evaluation.

QUALITATIVE PARAMETERS

During assessment of PHV stenosis, first we evaluate valve leaflet/occluder, presence of calcification or other abnormal structures like pannus or thrombus in relation to prosthesis, valve sewing ring integrity and rocking motion. Doppler assessment of the valve to assess peak velocity and maximum pressure gradient, mean PG, velocity time integral/Doppler velocity index, pressure half time in mitral and tricuspid valve, effective orifice area (EOA), presence, location and severity of regurgitation. After these, we assemble data regarding LV and RV size, function and hypertrophy, LA and RA size, coexistent valvular disease, pulmonary artery pressure. Echocardiography data is compared to immediate post-operative studies if available.

First-line imaging for PHV evaluation is 2 D TTE, should be added for complete evaluation of PHV. The complete echocardiographic imaging of the PHV includes multiple views like parasternal long axis, parasternal short axis, apical 4 chamber view and some off axis views (Figure 2).

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Table 1: Types of prosthetic heart valves

<table>
<thead>
<tr>
<th>Mechanical</th>
<th>Biologic</th>
<th>Stentless</th>
<th>Percutaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bileaflet St Jude</td>
<td>Porcine xenograft</td>
<td>Medtronic Freestyle</td>
<td>Expanded over a balloon</td>
</tr>
<tr>
<td>On-X</td>
<td>Medtronic Mosaic</td>
<td>Edwards Prima Plus</td>
<td>Edwards Sapiens</td>
</tr>
<tr>
<td>ATS</td>
<td>Hancock</td>
<td>Jena Valve</td>
<td>Lotus</td>
</tr>
<tr>
<td>Carbomedics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single tilting disc Medtronic Hall</td>
<td>Pericardial xenograft</td>
<td>Self-expandable</td>
<td></td>
</tr>
<tr>
<td>Sri Chitra</td>
<td>Carpentier Edwards Magna</td>
<td>- Medtronic Core Valve</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CE perimount</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caged-ball</td>
<td>Homograft</td>
<td>(allograft)</td>
<td></td>
</tr>
<tr>
<td>Starr-Edwards</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

valves.

Most frequently implanted mechanical valve is bileaflet PHV but tilting disc valves are still used. Though Ball in cage PHVs are not available now but still require echocardiography. Various designs of mechanical valves differ in the composition of pyrolitic carbon shape and opening angle of leaflet design, pivots, size and shape of housing and design of sewing ring.

PHVs also differ by their implantation position relative to the valve annulus mainly in aortic position i.e., intra-annular position, partially supra-annular and wholly supra-annular. Supra-annular position of PHV is used to maximize the orifice area of PHV.

Ideal PHV should have:

- Optimal hemodynamics
- Non obstructive in systole
- Competent in diastole
- Non thrombogenicity
- Durability
- Ease of insertion
- Resistance to infection
- Low noise level

None of the PHV available today, fulfill all the above criteria.

COMPREHENSIVE EVALUATION OF THE PATIENT WITH PROSTHETIC HEART VALVES

To evaluate a patient with PHV, stepwise approach is advisable. Take clinical information about date of valve replacement, type and size of PHV, height weight, body surface area, BMI of the patient, blood pressure and heart rate, symptoms and signs of the clinical condition.

Imaging of the valves to assess the motion of cusps, leaflets or occluder, presence of calcification or other abnormal structures like pannus or thrombus in relation to prosthesis, valve sewing ring integrity and rocking motion. Doppler assessment of the valve to assess peak velocity and maximum pressure gradient, mean PG, velocity time integral/Doppler velocity index, pressure half time in mitral and tricuspid valve, effective orifice area (EOA), presence, location and severity of regurgitation. After these, we assemble data regarding LV and RV size, function and hypertrophy, LA and RA size, coexistent valvular disease, pulmonary artery pressure. Echocardiography data is compared to immediate post-operative studies if available.
from the native valves. Bright echos on the cusps are indicative of calcification. In case of PHV thrombosis, there is immobility or reduced mobility of leaflets and presence of thrombus on either side of prosthesis. Pannus formation also leads to progressive obstruction which is usually more echo-dense than thrombus. There may be presence of endocarditis vegetations. TEE and 3D echo helps in more detailed evaluation of PHV.

During echocardiographic assessment of PHV some abnormal spontaneous echos may be found. These are

1. Spontaneous echo contrast (SEC) which is smoke like echos, caused by increased RBC aggregation. This occurs in slow flow states, left atrial dilation, AF or pathological mitral valve obstruction.
2. Microbubbles, are discontinuous stream of rounded, strongly echogenic and fast moving echos. These are formed at inflow zone of the valve when flow velocity and pressure suddenly fall at the time of closing of prosthetic valve.
3. Strands are thin, mildly echogenic, filamentous structures of several millimeters length, moving independently from the PHV. Their cause and management are not known. These are more commonly found during TEE for finding source of embolism. Their embolic potential is not clear.
4. Sutures are seen at the periphery of sewing ring in PHV as linear, thick, bright, multiple and evenly spaced, immobile echos.
5. Prosthetic valve dehiscence is characterized by a rocking motion of the entire prosthesis (Figure 5).
6. An annular abscess, on echo may be recognized as an echo-lucent, irregular shaped area adjacent to sewing ring.

FLOW CHARACTERISTICS OF PHV
Mechanical prosthetic valves, which are functioning normally, can produce some obstruction to blood flow - closure backflow, leakage backflow. Design of PHV influences the extent of obstruction and leakage. For example Ball in cage valve produce more obstruction and little leakage.

In case of bio-prosthetic valve, these normally show little or no leakage.

Homografts → No obstruction
Autografts → Present
Unstented bio-
prosthetic valve
Stented bio-
prosthetic valve → Mild obstruction

QUANTITATIVE PARAMETERS
Purpose of Doppler assessment across the prosthetic valve is to look for the pattern of flow which is unique for each PHV. Quantitative assessment of velocity and gradients and detection of abnormal regurgitation. Basic principles of Doppler assessment is same as for native valves.

Following parameters are measured for the prosthetic valve assessment
- Trans-prosthetic velocity and pressure gradient.
- Trans-prosthetic jet contour and acceleration time.
- Doppler velocity index (DVI)
- Effective orifice area (EOA)
- Pressure half time (PHT)
- Prosthetic-patient mismatch (PPM)

Trans Prosthetic Velocity and Gradient
To calculate flow velocity through the prosthetic valve, pulsed wave (PW), continuous wave (CW) and color Doppler are utilized in a similar way as for the native valves. Data recorded in multiple windows is taken in order to minimize angulation between the Doppler beam and flow direction and to obtain the highest velocity. The flow is eccentric for
monoleaflet valve while there are three separate jets in bileaflet PHV. Sometimes we overestimate the jet velocity gradients because of the finding of an abnormally high jet velocity by CW Doppler through the smaller central orifice of bileaflet mechanical in aortic or mitral position.

Because of various reasons, flow velocities are higher in normal functioning prosthetic valves and make them inherently stenotic. These are:

- Smaller sewing ring.
- Growing age of the patient.
- EOA is significantly smaller than area of sewing ring.
- Occluder mechanism occupies central space.
- Preservation process for leaflets in bio-prosthesis make them stiffer.

Normal pressure gradients across various PHVs in mitral and aortic position are depicted in Table 2 Figure 6 & 7.

**Trans Prosthetic Jet Contour and Acceleration Time**

This is a very helpful parameter to evaluate prosthetic heart valve function. For prosthetic aortic valve, normally the CW flow velocity contour is usually of triangular shape with early peaking of the velocity and shorter acceleration time (<80 ms). In conditions of prosthetic aortic valve stenosis contour becomes more rounded with the velocity peaking in mid ejection with longer acceleration time.

In case of aortic PHV, gradient changes with a change in stroke volume, and stroke volume is determined by patient’s BSA. Thus, among different patients with different BSA gradients differ even with same valve type and size. For this, we

**Table 2: Normal gradients for prosthetic heart valves**

<table>
<thead>
<tr>
<th>MITRAL PHV: NORMAL MEAN PG</th>
<th>AORTIC PHV: NORMAL MEAN PG</th>
</tr>
</thead>
<tbody>
<tr>
<td>VALVE TYPE</td>
<td>MECHANICAL</td>
</tr>
<tr>
<td></td>
<td>Bileaflet (St Jude)</td>
</tr>
<tr>
<td>Gradient</td>
<td>4±1</td>
</tr>
<tr>
<td>21</td>
<td>14 (10-30)</td>
</tr>
<tr>
<td>25</td>
<td>12 (5-30)</td>
</tr>
<tr>
<td>29</td>
<td>10 (5-15)</td>
</tr>
<tr>
<td>31</td>
<td>10 (5-15)</td>
</tr>
</tbody>
</table>
Perform a baseline echocardiogram after 1-2 months of PHV implantation and on repeat echocardiogram, if increase in mean gradient is more than 20 mmHg, it signifies pathologic obstruction.

In case of mitral prosthesis, we should interpret pressure gradient across PHV, taking into account the heart rate. Because, increase in heart rate causes decrease in duration of diastole, which may have a profound influence on pressure gradient. At the same time, we should consider about pressure half time (PHT). A low PHT with high gradient is not a sign of pathologic obstruction, it rather indicates high flow rate across PHV.

For PHV in mitral position, the condition is reversed. For this, initially the contour is parabolic with longer acceleration time and late peaking of velocity in mid ejection. As severity of obstruction increases, contour becomes triangular with early peaking of velocity and shorter acceleration time.

### DOPPLER VELOCITY INDEX (DVI)

When reliable measure of the LVOT diameter cannot be obtained to calculate the EOA with help of continuity equation method, DVI helps to screen the PHV stenosis in that situation. For PHV in aortic position, DVI can be calculated as the ratio of velocity time integral (VTI) of left ventricular outflow tract (LVOT) and velocity integral of trans-prosthetic peak velocity and gradient using CW Doppler.

\[
\text{DVI}_{\text{PrAV}} = \frac{\text{VTI}_{\text{LVOT}}}{\text{VTI}_{\text{PrAV}}}
\]

For PHV in mitral position, DVI should be more than 0.3, while for mitral valve prosthesis it should be less than 2.2.

### Effective Orifice Area (EOA)

EOA is a reflection of the minimal cross sectional area (CSA) of the trans-prosthetic flow jet. For both aortic and mitral prosthetic heart valves, EOA is calculated by continuity equation as:

\[
\text{EOA}_{\text{PrAV}} = \frac{\text{stroke volume}}{\text{VTI}_{\text{PrAV}}}
\]

\[
\text{EOA}_{\text{PrMV}} = \frac{\text{CSA}_{\text{LVOT}} \times \text{VTI}_{\text{LVOT}}}{\text{VTI}_{\text{PrMV}}}
\]

Where CSA is cross sectional area of LVOT which is derived by diameter measurement just beneath the prosthetic aortic valve in PLAX view. VTI LVOT is calculated by PW Doppler in apical five chamber view. It is important to locate the PW Doppler sample volume adjacent to the prosthesis.

VTI PrAV is calculated from the same signal that are used to measure trans-prosthetic peak velocity and gradient using CW Doppler.

Calculation of EOA for prosthetic mitral valve can be done as

\[
\text{EOA}_{\text{PrMV}} = \frac{\text{stroke volume}}{\text{VTI}_{\text{PrMV}}}
\]

where VTI PrMV is calculated from

---

Table 3: Doppler parameter of prosthetic mitral valve function (PrMV)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Possible Stenosis</th>
<th>Significant Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak velocity (m/s)</td>
<td>&lt;1.9</td>
<td>1.9-2.5</td>
<td>≥2.5</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>≤5</td>
<td>6-10</td>
<td>&gt;10</td>
</tr>
<tr>
<td>PHT (ms)</td>
<td>&lt;130</td>
<td>130-200</td>
<td>&gt;200</td>
</tr>
<tr>
<td>VTI_{PrMV}/VTI_{LVOT}</td>
<td>&lt;2.2</td>
<td>2.2-2.5</td>
<td>&gt;2.5</td>
</tr>
<tr>
<td>EOA (cm²)</td>
<td>≥2.0</td>
<td>1-2</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Adapted from JASE 2009; 22(9):996.

Table 4: Doppler parameters of prosthetic aortic valve function (PrAV)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Possible Stenosis</th>
<th>Significant Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak-Velocity (m/s)</td>
<td>&lt;3</td>
<td>3-4</td>
<td>&gt;4</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>&lt;20</td>
<td>20-35</td>
<td>&gt;35</td>
</tr>
<tr>
<td>DVI</td>
<td>&gt;0.30</td>
<td>0.29-0.25</td>
<td>&lt;0.25</td>
</tr>
<tr>
<td>EOA</td>
<td>&gt;1.2</td>
<td>1.2-0.8</td>
<td>&lt;0.8</td>
</tr>
<tr>
<td>Contour of the jet</td>
<td>Triangular-early Peaking</td>
<td>Triangular-to Intermediate</td>
<td>Rounded, Symmetrical Contour</td>
</tr>
<tr>
<td>AT (ms)</td>
<td>&lt;80</td>
<td>80-100</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>

A report from the American Society of Echocardiography guidelines and standards committee and the task force on Prosthetic valves. DVI= Doppler Velocity index, EOA = Effective Valvular Orifice Area Adapted from JASE 2009;22(9):990.
the same signal used for measuring transprosthetic peak velocity and gradient using CW Doppler.

Table 3 & 4 show various parameters for prosthetic valve obstruction in aortic and mitral position Figure 6.

**Patient Prosthesis Mismatch (PPM)**

Abnormally high post-operative gradient across the prosthetic valve occurs when EOA of the prosthetic valve is too small in relation to the body size of the patient, even if the valve is functioning normally. This condition is referred as patient prosthesis mismatch (PPM). This condition may result in an abnormally high postoperative gradients i.e., mean gradient may be as high as more than 20 mmHg. This high gradient is not due to intrinsic prosthetic valve dysfunction.

To differentiate true prosthetic valve dysfunction from PPM we have to calculate projected indexed EOA (Table 5 & 6).

**Effects of PPM**

If there is post-operative PPM, it may adversely effect the patient’s health outcome. It may cause:

- Worse hemodynamics
- Slower or incomplete regression of LVH or
- LV dysfunction
- Worse NYHA class, exercise capacity and quality of life.
- More cardiac events
- Decreased short and long term survival associated with LV dysfunction.

PPM can be avoided largely by the calculation of projected indexed EOA of the PHV to be implanted. If PPM is anticipated we should choose for alternative prosthesis or consider root enlargement surgery.

We can suspect PPM if transprosthetic flow velocity and pressure gradient are increased despite normal morphology and movement of valve leaflets. Presence of lower measured indexed EOA and presence of high flow velocity and pressure gradient from the time early after surgery to anytime on subsequent echocardiography also points towards PPM.

**Table 5: Patient prosthetic mismatch**

<table>
<thead>
<tr>
<th>Prosthetic Valve Size, mm</th>
<th>19</th>
<th>21</th>
<th>23</th>
<th>25</th>
<th>27</th>
<th>29</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic stented bioprosthesis</td>
<td>Medtronic Freestyle</td>
<td>1.2±0.2</td>
<td>1.4±0.2</td>
<td>1.5±0.3</td>
<td>2.0±0.4</td>
<td>2.3±0.5</td>
</tr>
<tr>
<td>Mosaic</td>
<td>1.1±0.2</td>
<td>1.2±0.3</td>
<td>1.4±0.3</td>
<td>1.7±0.4</td>
<td>1.8±0.4</td>
<td>2.0±0.4</td>
</tr>
<tr>
<td>Hancock</td>
<td>1.2±0.1</td>
<td>1.2±0.2</td>
<td>1.5±0.2</td>
<td>1.6±0.2</td>
<td>1.6±0.2</td>
<td></td>
</tr>
<tr>
<td>Carpentier- Edwards Perimount</td>
<td>1.1±0.3</td>
<td>1.3±0.4</td>
<td>1.5±0.4</td>
<td>1.8±0.4</td>
<td>2.1±0.4</td>
<td>2.2±0.4</td>
</tr>
<tr>
<td>Magna*</td>
<td>1.3±0.3</td>
<td>1.7±0.3</td>
<td>2.1±0.4</td>
<td>2.3±0.5</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Biocor (Epic)*</td>
<td>1.3±0.3</td>
<td>1.6±0.3</td>
<td>1.8±0.4</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Metroflow*</td>
<td>1.1±0.1</td>
<td>1.3±0.1</td>
<td>1.5±0.2</td>
<td>1.8±0.2</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

**Effects:**

- Reduced short and long term survival specially if with LV dysfunction.
- Less regression of LVH.
- Increased cardiac events.
- Less improvement of functional class.

**Table 6: Normal reference value of EOA indexed for the aortic prosthesis**

<table>
<thead>
<tr>
<th>Prosthetic Valve Size, mm</th>
<th>19</th>
<th>21</th>
<th>23</th>
<th>25</th>
<th>27</th>
<th>29</th>
</tr>
</thead>
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<tr>
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<td>2.0±0.4</td>
<td>2.3±0.5</td>
</tr>
<tr>
<td>Mosaic</td>
<td>1.1±0.2</td>
<td>1.2±0.3</td>
<td>1.4±0.3</td>
<td>1.7±0.4</td>
<td>1.8±0.4</td>
<td>2.0±0.4</td>
</tr>
<tr>
<td>Hancock</td>
<td>1.2±0.1</td>
<td>1.2±0.2</td>
<td>1.5±0.2</td>
<td>1.6±0.2</td>
<td>1.6±0.2</td>
<td></td>
</tr>
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<td>1.1±0.3</td>
<td>1.3±0.4</td>
<td>1.5±0.4</td>
<td>1.8±0.4</td>
<td>2.1±0.4</td>
<td>2.2±0.4</td>
</tr>
<tr>
<td>Magna*</td>
<td>1.3±0.3</td>
<td>1.7±0.3</td>
<td>2.1±0.4</td>
<td>2.3±0.5</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Biocor (Epic)*</td>
<td>1.3±0.3</td>
<td>1.6±0.3</td>
<td>1.8±0.4</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Metroflow*</td>
<td>1.1±0.1</td>
<td>1.3±0.1</td>
<td>1.5±0.2</td>
<td>1.8±0.2</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

EOA is expressed as mean values available in the literature.

*These results are based on a limited number of patients and this should be interpreted with caution.
Assessment of Pathologic Leakage of Prosthetic Valves

Mechanical prosthesis normally have closure and leakage backflow pattern which are dependent of prosthesis design. Doppler appearance of the jets help in distinguishing pathologic regurgitation from normal backflow. Normal closure and leakage backflow jets are low velocity, non aliasing jets of a homogenous color. In contrast, pathologic jets are more turbulent and extensive and eccentric (Figure 8).

Pathologic regurgitation in mechanical valves is caused by valve dehiscence or interference in disc closure by thrombus or vegetation, while in bio-prosthetic valves it can be caused by prosthetic dehiscence or leaflet degeneration.

Doppler Assessment of Severity of Regurgitation of PHV at Mitral Position

Enlarged LV size and any structural abnormality of prosthetic valve during TTE, can be the earliest indication of prosthetic valve dysfunction. Assessment of severity of MR in prosthetic mitral valve is a complex and difficult task because of absence of a single quantitative parameter that can be applied to all patients. Prosthetic MR evaluation is difficult by TTE, while prosthetic AR evaluation is difficult by TEE.

Parameters for Severity Assessment

Flow convergence: Minimal and large flow convergence are defined as convergence radius less than 0.4 and more than 0.9 cm for central jet respectively. For eccentric jet it may be higher. During systole, if flow convergence is large in LV side of prosthetic mitral valve, it denotes severe regurgitation while no or minimal flow convergence indicates mild prosthetic MR.

Jet density and jet contour: By using CW Doppler, we can evaluate jet density and jet contour of regurgitant jet which helps in assessing severity of regurgitation.

Retrograde systolic flow in pulmonary veins: Prosthetic MR can also be assessed by retrograde systolic flow in pulmonary veins. Severe MR is associated with swirling motion of jet within the LA and retrograde systolic flow in pulmonary veins, that can be assessed by TEE accurately.

Proximal iso-velocity area (PISA): Prosthetic MR is usually eccentric or consists of multiple jets thus, the PISA can’t be used, instead volumetric method for quantification of prosthetic MR is preferred.

Jet area: We measure jet and calculate the percentage with respect to LA area. If jet area is less than 4 cm² or less than 20% of LA, it indicates mild regurgitation but if jet area is more than 8 cm² or more than 40% of LA, it is indicative of severe regurgitation.

Vena contracta (VC): It is narrowest central flow region of a jet or just downstream to the orifice of regurgitant valve. It is smaller than the anatomic regurgitant orifice. Width of the VC is less than 3, 3-6 and more than 6 mm indicates respectively mild, moderate and severe regurgitation.

Quantitative Parameters for Assessment of Prosthetic MR Regurgitant Volume and Regurgitant Fraction (RV and RF)

The amount of blood leaking back into LA during systole through MV is regurgitant volume (RV). For mild, moderate and severe regurgitation it is less than 30, 30-59 ad more than 60 ml/beat respectively. The percentage of blood that regurgitates back through MV, due to MR is regurgitant fraction (RF) for mild, moderate and severe it is less than 30, 30-49 and more than 50% respectively. These are helpful in multiple and eccentric jets. They give information about lesion severity and volume overload status.

RV = stroke volume MV – stroke volume Non regurgitant valve

Effective Regurgitation Orifice Area (EROA)

It is the ratio of regurgitant volume (RV)/Regurgitant jet velocity time integral. It is less than 0.20, 0.20-0.49 and more than 0.50 cm² respectively for mild, moderate and severe regurgitation (Table 7).

Prosthetic Aortic Valve Regurgitation

Assessment of severity of PHV regurgitation at aortic position is done in a similar way as for native valves.

Color Doppler Evaluation

A ratio of regurgitant jet diameter and Left ventricular outflow tract (LVOT) diameter from PLAX view, less than 25%, 25-65% and more than 65% indicate mild, moderate and severe
regurgitation respectively. A ratio of jet area and LVOT area in PSAX view also helps in assessing severity. But, we can overestimate severity in case of eccentric or crescent shaped jets and under estimate in case of jets impinging on LVOT wall and anterior mitral leaflets, by using this method.

For semi-quantitative evaluation of paravalvular AR, careful imaging of the neck of the jet in PSAX view at the level of sewing ring or stent is required for defining circumferential extent (Figure 9).

A jet occupying less than 10%, 10-20% and more than 20% of the sewing ring circumference indicate mild, moderate and severe regurgitation respectively. If more than 40% of the circumference i.e., rocking movement of prosthesis it suggests dehiscence. TEE is helpful in case of multiple jets. Qualitative assessment based on proximal isovelocity surface area (PISA) is difficult to apply for mechanical aortic prosthetic valve. When assessable, usually in bioprostheses with central regurgitant jet, imaging of the flow convergence zone is done mainly in apical 3 or 5 chamber or PLAX views. Regurgitant volume, regurgitant fraction and EROA are obtained from standard formulas. RV more than 60 ml, RF more than 50% and EROA more than 30 mm² indicate severe prosthetic AR.

**SPECTRAL DOPPLER PARAMETERS**

These parameters are less affected by position shadowing and artifacts of prosthesis. Thus, these are very useful in case of PHV regurgitation. Right parasternal window is used for eccentric jets. The pressure halftime (PHT) of CW Doppler of regurgitant jet is useful when PHT is less than 200 ms, indicating severe AR or more than 500 ms indicating mild AR. But, values of 200-500 ms are less specific because these are influenced by other variable like heart rate, LV compliance and LV pressures and acuteness of AR. In acute AR, PHT is shorter.

**Diastolic flow reversal in descending aorta**

Sample volume is placed just distal to the origin of left subclavian artery, for imaging diastolic flow reversal in descending aorta. PW Doppler is aligned along the major axis of aorta, Doppler filter is decreased to lowest setting and velocity scale is set to 60-80 cm/s. In mild AR, reversal of flow is limited to early diastole and is brief. As the severity of AR increases, duration and velocity of flow reversal also increases. The presence of holo-diastolic flow reversal indicates atleast moderate AR, but when this is associated with end-diastolic flow of more than 20 m/s, it indicates severe AR (Table 8).

**TRANSVERSE AORTIC VALVE REPLACEMENT (TAVR)**

This is a minimally invasive procedure and it replaces the valve without removing older damaged valve. Edwards the Sapien valve and Core valve system are two devices used for TAVR (Figure 3).

In Edwards Sapien valve, three pericardial leaflets are mounted within a balloon expandable stent, while in Core valve revolving system, three pericardial leaflets are mounted in a self expanding nitinol frame. Transfemoral or transapical approach for TAVR, are commonly used. Most common drawback of TAVR is AR, which may be trans-valvular or paravalvular or both occurring together. Recently, supraskirtal AR, a third form of AR associated with TAVR has also been described (Figure 10).

**PROSTHETIC PULMONARY VALVE**

Congenital heart disease, is the main indication where prosthetic pulmonary valve or homograft is generally implanted. These valves may also undergo stenosis or insufficiency.

Clues indicative of PHV stenosis in pulmonary position on echocardiography are:
- Marked thickening of the cusps.
- Immobility of the cusps
- Trans-valvular peak velocity across prosthetic valve more than 3 m/s or across homograft more than 2 m/s.
- Depressed right ventricular function and right ventricular pressure overload.

Clues indicative of severe insufficiency of PHV in pulmonary position are:
- Right ventricular volume overload
- Diastolic flattening and paradoxical movement of the interventricular septum.

**Prosthetic Tricuspid Valve**

Tricuspid prosthetic valves are assed by parasternal, low parasternal, apical and subcostal views. Clues indicative of stenosis of PHV in tricuspid position are:
- Thickening or abnormal morphology of cusps.
- Reduced mobility or immobility of cusps
- Peak velocity across valve more than 1.7 m/s
- Mean gradient more than 6 mmHg and
- Pressure half time more than 230 ms.

Tricuspid prosthetic velocity varies with cycle length and respiration thus, we take a minimum of 5 cardiac cycles and get average of these, Clues for tricuspid prosthetic regurgitation.
- Peak velocity across valve more than 1.7 m/s.
- Mean gradient more than 6 mmHg.
- CW Doppler shows a dense spectral recording with a triangular shape and velocity peaking early.
- Elevated peak and mean diastolic pressure gradients.

**OTHER MODALITIES FOR PHV EVALUATION**

**Cinefluoroscopy**

Has limited value in bioprosthetic valves but can be easily applied for mechanical valves. The valvular leaflet mobility and valvular ring motion is evaluated with the help of cinefluoroscopy.

For fluoroscopy study, patient has to lie down in supine position. Three projections are used for viewing PHVs.

- **In situ** projections: Radiographic beam is projected postero-anterior (O degree) and lateral (90 degree) to evaluate orientation of the valves.
- **In profile** projection: Radiographic beam is projected parallel to both the valve ring plane and the tilting axis of disc. It helps in calculation of opening and closing angles.

**Cardiac CT**

There is no definitive indication for CT in evaluation of PHVs dysfunction, thus not used routinely. But there are some conditions where CT may be very helpful. These are

- In distinguishing thrombus from pannus.
- In quantifying severity of stenosis in a bioprosthesis by planimetry.
- In identifying paravalvular regurgitation and malcoaptation.
- Ventricular or atrial dilation or stasis identification, which are morphological consequences of obstruction or regurgitant lesions of PHVs.
- Calcification on CT, aids in early detection of failure of biologic PHV.

**Cardiac MRI**

When TEE is undesirable or non-diagnostic it can be used as a complementary method for assessing the function of PHVs. It is an excellent technique for assessment of cardiac chamber volumes and flow patterns. PHV anatomy can be assessed by short axis, to 2, 3 and 4 chamber long axis views with oblique long axis view in the line of coaptation. For obtaining blood flow patterns and velocity, phase contrast
velocity mapping by CMR is done. Thus it may be very helpful in assessing regurgitation of PHV.

**Cardiac Catheterization**

It helps in measuring flow velocity and pressure gradients across the PHV and assessing flow patterns. These parameters help in calculation of EOA by Gorlin formula. It is mainly useful in bioprosthetic valve because it may cause complications like regurgitation in case of mechanical valves when catheter is passed across PHV.

When invasive mitral prosthetic gradient is required, we measure directly the LA pressure by transseptal approach because measurement of wedge pressure can overestimate pressure gradients and underestimate EOA.

**COMPLICATION OF PHVS**

**Early Complications**
1. Valvular dysfunction - due to technical challenges during surgery or early infection
2. Paravalvular leak
3. Early prosthetic thromboembolism
4. Acute endocarditis

**Late Complications**
1. Late valvular dysfunction
2. Thrombus and thromboembolism
3. Pannus formation
4. Valve degeneration
5. Annular abscess
6. Endocarditis
7. Hemolysis
8. Dehiscence
9. PPM
10. Primary failure

**ENDOCARDITIS**

In a stable patient with PHV and fever, first we should exclude other causes of fever. If we are unable to get a definitive cause, we perform echocardiography for endocarditis. On the other hand, if the patient is severely ill or there is medium or high clinical suspicion for endocarditis, we perform echocardiography (Figure 11).

Initially vegetations are formed in a ring area, from where it spread to involve components of PHVs and impair opening and closing of leaflets, vegetations are identified as an irregular, freely mobile mass of low echogenicity on echocardiography.

**Complications of Endocarditis**
1. Abscess formation, which may lead to
   - Conduction defect if it involves IVS
   - Shunt between two chambers
2. Suture dehiscence and paravalvular regurgitation in all PHVs
3. Valve destruction

If we are unable to find a significant lesion of endocarditis in TEE, but the clinical suspicion is high, we should use TEE. Because TEE is superior in detecting vegetations and perivalvular abscess in posterior aortic root than TTE. Anterior structures are better seen by TTE and posterior structures by TEE. Despite combined approach, a small percentage of cases can be missed. A repeat study after 7-10 days should be recommended in such circumstances.

**PROSTHETIC VALVE THROMBUS AND PANNUS AND THEIR DIFFERENTIATION VALVE THROMBOSIS**

Mechanical valves are more prone for thrombus formation than bioprosthetic valves (Figure 12).

Usually, thrombus is associated with obstruction, regurgitation and embolism, but sometimes it may be silent. Thrombus formation leads to significant obstruction, which may be catastrophic. It is treated by redo operation and fibrinolysis. Fibrinolysis is treatment of choice for tricuspid valve thrombosis. TEE and Doppler are used to assess serially for success of thrombolytic therapy and improved hemodynamics. If on TEE, thrombus area is more than 0.85 cm², it confers a higher risk of embolism.
and death associated with thrombolysis (Table 11).

**PANNUS**

After prosthetic valve implantation, a membrane of granulation tissue as a response to healing, forms which may cause obstruction. This granulation tissue is called pannus.

Per year the incidence of PHV obstruction is 4%. Among these:

- Pure thrombus (75%)
- Pure pannus (10%)
- Combination of both (12%)

Table 9 Figure 13.

**TEE FOR EVALUATION OF PHV**

Multiplane TEE is considered the diagnostic technique of choice for evaluation of type of prosthesis, assessment of its function and diagnosing dysfunction. With the combination of Doppler and color doppler imaging, the ability of TEE to integrate the structural information and hemodynamic function is unparalleled. The increased resolution with TEE is advantageous in defining the
cause of PHV dysfunction (Table 10).

Clinical role of TEE include evaluation of native valve, intraoperative evaluation and guidance apart from diagnosing valve dysfunction post operatively. TEE can distinguish the normal/abnormal movement of leaflet(s)/occluder, abnormal movement of valve or dehiscence of PHV annulus, vegetation, calcification, thrombus and pannus.

**Technical Consideration**

Due to metallic or polymeric components of PHV it is difficult to image the structure posterior to PHV. However technical modifications are helpful.

1. Decreasing the transmit gain
2. Multislice imaging
3. Mid esophageal TEE will not show aortic valve PHV leaflets, however trans-gastric position can show the leaflet movement (Figure 4).

Ventricular side of MV prosthesis is better seen from trans-gastric position.

A systematic TEE examination of PHV includes
- The recognition of type of PHV.
- Proper seating of PHV within the native annulus.
- Normal blood flow pattern through the valve.
- Absence or presence of paravalvular leak and its significance.

Doppler echocardiography is used to estimate the trans-valvular gradient across PHVs which have central jet. While caged ball prosthesis, occluder changes the direction of blood flow through this direction and Bernoulli’s equation does not estimate a correct mean PG. For gradient measurement it is important to align the ultrasound beam to transprosthetic flow. It is easily determined in mid esophageal TEE 60 degree, 90 degree or 120 degree in angles in patients with mitral valve PHV. While in aortic PHV, it is better measured in transgastric views at 90 degree or 120 degree.

Most commonly utilized bileaflet mechanical valve due to its durability record, and wider effective orifice area, movement of both leaflets in opening closing is confirmed. Two linear shadows are well recognized in open position in short axis within circular annulus. Multiplane rotation through the valve generates a cross sectional plane perpendicular to two leaflets which permits to show movement of both leaflets simultaneously. Next any abnormal movement of sewing ring is seen. Valve dehiscence is normally associated with paravalvular regurgitation originating outside annulus/sewing ring. Valve dehiscence is usually caused due to incomplete fixation of valve in severely calcified valve during surgery. Other important reason is complication of endocarditis. Valve dehiscence and endocarditis is better observed by multiplane TEE.

Small amount of regurgitation is normal for bileaflet PHV. These small jets regurgitant are usually referred as cleansing jets. Usually this jet is at hinge points but small regurgitant jet may be present at closing site of leaflets along the annulus.

Intraoperative pathological valvular regurgitation is due to malfunction of valve due to retained tissue that prevents valve closure, or misplaced suture interfering with the leaflet movement.

**Paravalvular Regurgitation is Always Pathologic**

Cage ball valve produce large acoustic shadowing and its motion is best seen in long axis view, color Doppler shows blood flow in between the wired stents.

Tilting disc PHV consists of a disc which is supported by stents. Single disc opens 60-80 degree to form two orifices of different size and shape. These valves also have low profile and provide larger ejection orifice area. Proper tilting angle is confirmed through multiplane TEE examination. Color Doppler shows a small leakage backflow jet at hinge point or along in the site of contact of disc and annulus strut fracture and is a serious complication and can lead to disc embolization.

Biological valves are reserved for younger patients or patients who do not tolerate anticoagulation. Stented porcine valve has slightly lesser EOA compared to bileaflet PHVs and they have favorable acoustic profile.

Pericardial bio-prosthesis are indistinguishable from the stented porcine valve.

Stentless bio-prostheses are useful in patients with native valve annulus less than 20 mm in diameter. Their profile is better than stented PHVs however, intraoperatively the matching of annulus size and alignment of annular plane and ruling out dilatation of ascending aorta is important. Sino-tubular junction should be within 10% of annulus of stentless PHV. However, the thickness of vessel is increased due to overlap. Trace or mild paravalvular leak is present in 25% of these valves. These regurgitant jets are clinically insignificant.

Allografts are also to be matched to annular size to avoid para-valvular leak or valve incompetence. Allografts are also indistinguishable from native aortic root or valve.

Prosthetic valve complications are better recognized by TEE. Bio-prosthetic valve regurgitation is commonly associated with degenerative changes, leaflet calcification, tears, prolapse and leaflets obstruction due to endocarditis.

In mechanical PHV the pathological regurgitation is result of pannus

### Table 10: Use of TEE for prosthetic heart valve

<table>
<thead>
<tr>
<th>TEE before valve replacement</th>
<th>TEE after valve replacement</th>
<th>TEE for PHV dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verify disease of native valve</td>
<td>Movements of leaflet/occluder</td>
<td>Type of PHV</td>
</tr>
<tr>
<td>Extent of annular calcification</td>
<td>Valvular/paravalvular regurgitation</td>
<td>Valve degeneration or</td>
</tr>
<tr>
<td>Annular diameter of native valve</td>
<td>No air in cardiac chambers</td>
<td>Calcification Thrombus/</td>
</tr>
<tr>
<td>Feasibility of valve repair</td>
<td>No LVOT obstruction by stents or subvalvular apparatus</td>
<td>pannus/vegetation</td>
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<td>Quantification of</td>
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<td>Quantification of PHV</td>
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<td>stenosis</td>
</tr>
</tbody>
</table>
formation, thrombus, vegetation or valves component obstructing the complete closure of occluder. Clinical severity can be checked by measuring vena contracta and calculating regurgitant volume or effective regurgitant orifice.

Paravalvular leak is due to incomplete fixation of sewing ring to native annulus. Rocking movement is produced by valve dehiscence which is a visible separation of prosthetic valve and native anular separation.

PHV stenosis is produced by thrombus, pannus or vegetation. Thrombus is usually a result of inadequate anticoagulation. It interferes with closing and opening movement of leaflets, size and extent of thrombosis can be better seen with TEE. Thrombus size less than 0.85cm² confers lower risk of embolism and death related to thrombolysis. Size of thrombus can be determined by TEE. Pannus can be differentiated from thrombus with the help of TEE examination.

TEE is a better technique to detect vegetation, annular abscess etc. It is important to use mid-esophageal and trans-gastric view to see both sides of PHV. Left ventricular obstruction is rare complication specially due to chordae sparing or it can happen in stented porcine valve due to stent projecting in LVOT. Trans-gastric view provides means to image LVOT after MV replacement to estimate LVOT pressure gradient.

3D ECHO SPECIALLY 3D TEE
Current 3D probes are superior to earlier TEE probes to reconstruct the image. Earlier 3D techniques were time consuming, tedious and extensive post-processing was required. Recent advances in real-time 3D imaging have propelled 3D TEE into clinical practice from the research realm. It is possible to have real-time acquisition through matrix array, TEE transducer and online display of 3DTEE images. There is no need of offline reconstruction. R3DTEE has allowed improved visualization and assessment of prosthetic valves.

To acquire 3D images 2D examination is first used to locate best plane for imaging PHV.

Gain setting is optimized using narrow angled acquisition mode. Subsequently zoom mode with biplane imaging is used to focus PHV. Then volumetric volume acquisition is recorded. ECG gating is required and acquisition is done in 4-7 heart beats. Then cropping techniques are utilized to see various component of PHV. Rings leaflets, stents can be clearly visualized from both left atrial and left ventricular perspective.

In aortic, mechanical, biological or PHV, leaflet movement is poorly visualized. Similarly TV PHV leaflets are also poorly visualized. This is due to distance from transducers to aortic or TV, PHV. However, R3DTEE allows evaluation of valve components, ring, annulus, struts. Thrombus in relation to the prosthetic heart valve is recognized and differentiated from pannus. Size and location of thrombus helps in proper management (Table 11).

Acquisition of RT 3DTEE only require approximately 10 additional minutes.
RT3DTEE has shown to provide additional information to evaluate PHV endocarditis. Due to acquisition of wide angled, full volume data and ability to crop the images, deep anatomical structures can be clearly seen and displayed. PHV evaluation is possible in the angles which was not possible in 2D planar views. Enface view of PHV is useful in assessment of PHV endocarditis. It allows to see additional vegetation not seen in 2D planer view.

PARAVALVULAR REGURGITATION (PVL)
Paravalvular leaks are better recognized by RT3DTEE. It plays important role in
1. Evaluation of paravalvular regurgitation (size and location).
2. Guidance during intervention
3. Post intervention assessment

3D zoom mode provides enface views of both mitral and aortic PHVs. Mitral valve imaging from LA perspective is conventionally rotated so that aorta is at 12 O’clock and LAA appendage at 9 O’clock position. Dehiscence site is localized, shape and size and site of paravalvular leaking confirmed with use of 3 dimensional color flow. RT 3 D TEE provides a more accurate site and size of paravalvular leakage (PVL). It is important to decide the suitability of percutaneous closure of PVL vs surgical closure. RT 3D TEE also guides surgeon for size and site and adequacy of repair after coming
off bypass. Procedure of PVL closure is guided for route of approach to PVL. This approach can be antegrade or retrograde. Small PVL are occluded by amplatzer. PDA device while larger defects are closed by amplatzer ventricular septal device. Continuous guidance is provided during the percutaneous closure of PVL—selection of site of atrial septal puncture and guidance of catheter and device into PVL site.

LIMITATIONS

1. Poor visualization of anterior structures like aortic and tricuspid valve.
2. Suboptimal images during arrhythmia due to poor ECG triggering. This issue has been resolved by single beat acquisition mode.
3. Newer machines have increased frame rate, spatial and temporal resolution and moving structures like vegetations are better seen. Tissue drop outs can be interpreted as anatomic defect while increasing gain may result in blurry images. However experience as well as combining imaging to color and Doppler information helps to differentiate true and false defects.

CONCLUSION

Physicians taking care of prosthetic valve patients should be familiar with the characteristics of normal prosthetic valves. Various varieties of PHV’s have specific echo-cardiographic patterns and Doppler and color Doppler parameters. Deviations from normal pattern specially valve thrombosis, pannus and vegetation are easily recognized by trans-esophageal echo, and more specifically 3D real-time TEE. Paravalvular leak size and shape of regurgitant orifice is also recognized. 3D real-time TEE should be routinely applied along with other Doppler parameters for prosthetic valve evaluation.

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Mechanism of Hypertension

ALPANA RAIZADA, SHRIDHAR DWIVEDI

Abstract
Hypertension is expected to affect more than half of the adult population of the world and its consequences contribute significant morbidity and mortality across the globe. Despite widespread prevalence and aggressive research into its etiopathogenesis only about 5% of patients with hypertension have an identifiable cause. The complex multifactorial mechanisms leading to hypertension have resulted in an increased number of people with suboptimally controlled blood pressure in spite of the advances in antihypertensive drug therapy. Hypertension results from dynamic interactions between multiple genetic, physiological, psychological, and environmental factors. An improved understanding of these dynamic interactions may pave the path for more targeted interventions in the long run.

INTRODUCTION
Hypertension is a major modifiable risk factor for cardiovascular disease (CVD). The estimated global prevalence of hypertension is high. About 26% of the world’s adult population (972 million) had hypertension in the year 2000 which increased to 31% (1.39 billion) in 2010. Rates were higher in low- and middle-income (31.5%) than in high-income (28.5%) countries. Long-term projections suggest that, by 2025, 29 percent of adults worldwide would have hypertension (1.56 billion people globally). Despite extensive research over the past several decades, the etiology of most cases of adult hypertension is still unknown, and control of blood pressure is suboptimal in the general population especially in lower-income countries. In 2010, hypertension control was estimated to be 28% in high-income and 8% in middle- and low-income countries. Suboptimal control has been observed not just in general population but also in units dedicated to control of hypertension. Prevention and treatment of hypertension is an important public health challenge due to associated high morbidity, mortality and cost to the society.

PRIMARY HYPERTENSION
Primary, essential or idiopathic hypertension is defined as high blood pressure (BP) in which secondary causes such as renovascular disease, renal failure, pheochromocytoma, aldosteronism, monogenic hypertension or other causes of secondary hypertension are not present. Primary hypertension accounts for about 95% of all cases of hypertension. Primary hypertension is a heterogeneous disorder, with different patients having different causal factors that lead to high BP. The pathogenesis of primary hypertension is multifactorial and highly complex.

Keywords
hypertension mechanism
- genetic factors
- RAAS
- sympathetic tone
- obesity
- dietary salt
Factors that play an important role in the pathogenesis of hypertension include:
- Genetics
- Autonomic nervous system
- Renin-angiotensin-aldosterone system (RAAS)
- Obesity
- Dietary salt intake

A number of other factors have also been incriminated in causing hypertension namely, insulin resistance, high alcohol intake, aging, sedentary lifestyle, stress, low potassium intake, and low calcium intake (Figure 1).

**GENETIC FACTORS IN THE PATHOGENESIS OF HYPERTENSION**

Blood pressure is a classic quantitative genetic trait with family and twin studies estimating the heritability of blood pressure to about 30 to 50 percent. Thus genomics has the potential to contribute to the poorly understood pathogenesis of primary hypertension. The importance of genes in hypertension is underlined by the fact that hypertension is 2.4 times more common in subjects who have two hypertensive parents. The genetic contribution to blood pressure regulation is of two different types:

1. **Monogenic hypertension and rare genetic variants** – Rare mutations segregating in families can cause secondary hypertension, even in the absence of other risk factors ("monogenic" hypertension, such as Liddle's syndrome). Once a monogenic form of hypertension is identified, these cases should be labelled as secondary rather than primary hypertension.

2. **Primary hypertension and common genetic variants** – There are possibly hundreds to thousands of common genetic hypertension risk variants that are modulated by environmental factors such as age, body mass index (BMI), sex, salt consumption etc. Therefore, primary hypertension cannot be due to one or only a few genetic variants, and there is no entity as the primary hypertension gene.

Genome-wide association studies (GWAS) have facilitated the understanding of the genetic basis of primary hypertension by easing out genotyping of hundreds of thousands of variants. This method searches the genome for small variations, called single nucleotide polymorphisms (SNPs) that occur more frequently in people with a particular disease than in people without that disease. Many studies have shown associations of gene polymorphisms and BP, but the genetic variants that contribute to essential hypertension remain unknown. Despite these inconsistent findings, it is believed that genetic factors may account for up to 30-50% of BP variance. Genetic factors also influence behavioural patterns, which might lead to BP elevation. For example, a tendency toward obesity or alcoholism is influenced by both genetic and environmental factors. Thus, the proportion of BP variance caused by inheritance is difficult to determine and may vary in different populations.
AUTONOMIC NERVOUS SYSTEM

One of the most widely accredited and tested hypotheses in cardiovascular research is that derangement of sympathetic and parasympathetic cardiovascular regulation leads to hypertension. Adrenergic reflexes modulate blood pressure over the short term and adrenergic function in association with hormonal and volume related factors contributes to the long-term regulation of arterial pressure (Figure 2).

Autonomic imbalance (increased sympathetic tone accompanied by reduced parasympathetic tone) contributes to the development and maintenance of hypertension through stimulation of the heart, peripheral vasculature, and kidneys, causing increased cardiac output, increased vascular resistance, and fluid retention. Evidence supporting role of autonomic imbalance is elucidated by results that sustained increases in heart rate are due mainly to decreased parasympathetic tone and that diastolic blood pressure relates more closely to vascular resistance (modulated by sympathetic tone) than to cardiac function.

The mechanisms of increased sympathetic nervous system activity in hypertension are complex and involve alterations in baroreflex and chemoreflex pathways at both peripheral and central levels. Also, chronic sympathetic stimulation induces vascular remodelling and left ventricular hypertrophy, presumably by direct and indirect actions of norepinephrine on its own receptors, as well as on release of various trophic factors, including transforming growth factor-β, insulin-like growth factor 1, and fibroblast growth factors.11 Circulating norepinephrine levels exhibit positive correlation with left ventricular mass, and reduced radial artery compliance (an index of vascular hypertrophy).12 Renal sympathetic stimulation is also increased in hypertensive patients compared with normotensive controls. Thus, sympathetic mechanisms contribute to the development of target organ damage, as well as to the pathogenesis of hypertension.

RENIN-ANGIOTENSIN-
ALDOSTERONE SYSTEM (RAAS)

The RAAS plays a dominant role in salt and water homeostasis and hence BP control. It is also an important therapeutic target. Granular cells in the juxtaglomerular apparatus synthesize and release renin.

Renin release is mediated by:
- Decreased afferent arteriolar (i.e. renal perfusion) pressure of any cause.
- Sympathetic nervous system activation (granular cell B-1 receptors).
- Decreased Na+ delivery to the distal tubule (sensed by the macula densa).
- Prostacyclin, ACTH.

Renin converts inactive angiotensinogen into angiotensin I, which, in turn, is converted by angiotensin converting enzyme (ACE) in the lungs to active angiotensin II (A2). A2 binds to two receptors AT-1 and AT-2.

ANGIOTENSIN

Angiotensin II increases blood pressure by various mechanisms like:
- Arteriolar vasoconstriction (and venular constriction to a lesser extent).
- Efferent renal arteriolar vasoconstriction.
- Aldosterone secretion.
- Adrenaline (epinephrine) release.
- Smooth muscle hypertrophy.
- Increased reabsorption of sodium in PCT.
- Inhibition of renin release (negative feedback loop).
- Renal mesangial cell growth and matrix expansion.
- Myocardial growth and matrix expansion.
- Stimulation of thirst and ADH release.

Most effects are mediated by the angiotensin type 1 (AT-1) receptor. Circulating angiotensin II binds vascular receptors, but locally released A2 works at tissue level in a paracrine fashion. Tissue concentrations do not correlate with systemic levels but may correlate better with disease pathogenesis.

The activity of local renin–angiotensin systems and alternative pathways of angiotensin II formation may make an important contribution to remodelling of resistance vessels and the development of target organ damage (including left ventricular hypertrophy, congestive heart failure, atherosclerosis, stroke, end-stage renal disease, myocardial infarction, and arterial aneurysm) in hypertensive persons.

ALDOSTERONE

Aldosterone synthesis occurs mainly in the zona glomerulosa of the adrenal cortex and is tightly regulated by the renin - angiotensin system (RAS) and electrolyte homeostasis (increased K+ or decreased Na+ intake increases aldosterone synthesis). Aldosterone acts at the collecting duct to promote Na+ retention and K+ excretion.
ANGIOTENSIN II AND OXIDATIVE STRESS
Angiotensin II also increases cardiovascular risk by stimulating oxidant production. This forms the basis of clinically important vasoprotective effects beyond lowering of blood pressure as exhibited by ACE inhibitors and ARBs which limit oxidative reactions in the vasculature by blocking the activation of NAD(P)H oxidase (Figure 3).

OBESITY AND INSULIN RESISTANCE
Obesity is an important cardiovascular health problem, the incidence and prevalence of which is reaching epidemic proportions in developed and developing countries. Apart from being hypertensinogenic obesity is also the cause of insulin resistance, adult-onset diabetes mellitus, left ventricular hypertrophy, hyperlipidemia, and atherosclerotic disease. It is estimated that at least 75% of the incidence of hypertension is related directly to obesity. Each 10% weight gain has been seen to be associated with a 6.5 mmHg increase in systolic BP. The relationship between BP and body fat is not just continuous throughout the entire range of body weight but is also evident from early childhood to old age.

The mechanism by which obesity raises BP is still incompletely understood. Several factors have been implicated in the pathogenesis of obesity related hypertension (Table 1).14 Increased BMI is associated with an increase in plasma volume and cardiac output; which can be decreased by weight loss in both normotensive and hypertensive subjects, even when sodium intake is kept relatively constant. However, BP in obese adolescents is sodium sensitive, and significant drop in mean BP can be achieved after shifting to a low-sodium diet. Loss of weight by dieting in these individuals decreased BP as well as salt sensitivity. The variables that best predicted sodium sensitivity were fasting plasma insulin, plasma aldosterone, and plasma norepinephrine, supporting the hypothesis that BP is sensitive to dietary sodium and that this sensitivity may be due to the combined effect of hyperinsulinemia, hyperaldosteronism, and increased activity of the sympathetic nervous system. It was also observed that exercise even without weight loss lowered BP especially in those who initially had high fasting insulin and whose insulin levels fell in response to exercise. Thus, exercise decreases plasma insulin by a different mechanism than loss of body weight and that decreasing insulin resistance by losing weight or exercising reduces BP.

DIETARY SALT INTAKE AND HYPERTENSION
The level of BP in an individual is a cumulative effect of several influences like genetics, environmental, physiologic and clinical genetic factors. Of these the most readily modifyable factor is dietary sodium intake which has a very important role in the pathogenesis of hypertension. More than 100 trials examining the relationship between sodium intake and BP have shown evidence that reduction in sodium intake is coupled with reduction in BP. This reduction is evident across all age groups in both hypertensive as
well and normotensive individuals. A reduced sodium intake has the potential to delay the onset of hypertension as well as blunt the age-related rise in BP and thus contribute to the overall reduction in cardiovascular disease risk.

"Salt sensitivity" is the term applied to the heterogeneous BP response to an increased sodium intake which may be influenced by age, gender, genetics and presence of certain clinical conditions like hypertension, diabetes, and chronic kidney disease. It has been shown that greater BP response to change in sodium intake has been seen in blacks as compared to whites, hypertensives as compared to nonhypertensives, and older persons as compared to younger adults.

There is positive correlation of total exchangeable sodium with arterial pressure. This increase in BP is not by increase in blood volume but by increase in peripheral resistance. High sodium and low potassium inhibit the sodium pump, increase intracellular sodium, and drive calcium into cells, which ultimately induces vascular smooth muscles contraction and increases peripheral vascular resistance. The hypothesis that in most cases of essential hypertension excessive salt intake leads to gene expression for hypertension is supported by the Framingham Offspring study cohort, which identified in 1.2% of the study participants a systolic blood pressure of 6 to 9 mmHg greater than that of the normotensive individuals.

The prevalence of hypertension is increasing by leaps and bounds. As most of the times an etiological diagnosis of hypertension remains elusive, therefore a better understanding of the mechanisms of hypertension may lead to more targeted therapies and can ultimately translate into greater reduction in hypertension-related cardiovascular disease morbidity and mortality.

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"U" wave

SR MITTAL

Abstract

U-wave is the wave between T wave and P wave. It is usually seen with slow heart rate and is most apparent in leads V_2 to V_4. Its polarity is same as that of T wave. Its amplitude is normally less than one third of the amplitude of T wave. Genesis of this wave is uncertain. A positive, low amplitude U wave is most often physiological. Prominent U wave is common in bradycardia and hypokalemia. Negative U wave is usually ischemic in origin.

(A) INTRODUCTION

U wave is the wave between T wave and P wave. Its genesis is not clear. Several hypotheses have been proposed but there is no consensus of opinion.

(B) PHYSIOLOGICAL U WAVE

U wave is a small wave after the end of T wave. It can be identified in all leads but is usually most apparent in leads V_2 to V_4 (Figure 1). It is better visible at slower heart rate (<65 beats/minute) and in elderly. Amplitude is normally less than 0.2mv. Amplitude varies directly with the amplitude of T wave. Normally it is less than 25% of the amplitude of T wave. Amplitude is also dependent on heart rate. There is inverse relationship between heart rate and U wave amplitude. i.e. U wave amplitude increases with decrease in heart rate. Normally the polarity of U wave is same as that of T wave. Therefore U wave is normally negative in lead aVR and at times in lead V_1 (Figure 2).

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Dr. SR Mittal is Head, Department of Cardiology at Mittal Hospital and Research Centre, Ajmer, Rajasthan
Clear U wave is not recognized in presence of atrial fibrillation due to wavy base line2 (Figure 3). However it can be visible in patients with straight line fibrillation with controlled ventricular rate (Figure 4). Sometimes in patients of atrial fibrillation, fibrillary waves may be confused with normal U wave and P wave (Figure 5A). Recording long lead helps in identifying the irregularity of rhythm and true nature of fibrillary waves (Figure 5B).

At times T wave may encroach on U wave making a T-U complex. In such a situation, it may be difficult to differentiate U wave from second peak of a notched T wave. Apices of a notched T wave are usually less than 0.15 second apart (Figure 6) where as the interval between the apices of T wave and U wave is usually more than 0.15 sec.2 Secondly, normal U wave is less than one third of the amplitude of T wave. Therefore, in a T-U complex, the second peak is much smaller than the first peak (Figure 7). On the contrary, second peak more than 50% of first peak strongly suggests a bifid T wave.

U wave is similar to P wave in appearance.1 In patients of atrial fibrillation with fast ventricular rate, it may be misinterpreted as a P wave if a QRS complex follows it (Figure 8). Irregularly irregular rhythm and absence of such pseudo P wave in most of the beats helps correct identification of atrial fibrillation. In patients with sinus bradycardia, U wave may be misinterpreted as additional P wave resulting in wrong diagnosis of 2:1. A-V block1 (Figure 9). Time interval between preceding P wave and U wave is however, different from the interval between U wave and following P wave (Figure 9). This gives a clue to identification of U wave.

(C) PROMINENT U WAVE

U wave is prominent in following conditions

(1) Hypokalemia- It is the commonest cause of prominent U wave (Figure 8, 9). It is associated with depression of ST segment and decreased amplitude of T wave. ECG changes may appear even when serum potassium concentration is within normal limits.5

(2) Hypocalcemia

(3) Hypomagnesemia

(4) Antiarrhythmic drugs e.g. Amiodarone, dofetilide

QT interval is prolonged with fusion of T and U waves forming a prominent and broad T-U fusion wave (Figure 12)

(5) Hypothyroidism

Sinus bradycardia, low voltage QRS and relative flattening of T wave are other findings (Figure 13)

(6) Hypothermia

(7) Inherited long QT syndrome type 3
ECG OF THE MONTH

Figure 8. Electrocardiogram showing U wave giving a false impression of a P wave during fast rate in a case of atrial fibrillation.

Figure 9. Diagrammatic representation comparing electrocardiographic findings (a) in a case of sinus bradycardia with prominent U wave (b) from a case of 2:1 A-V block.

Figure 10. Electrocardiogram from a patient of hypokalemia showing prominent U wave.

Figure 11. Electrocardiogram from a patient of hypokalemia showing prominent U wave.

Figure 12. Electrocardiogram showing fusion of T and U wave with prolongation of QT interval.

Figure 13. Electrocardiogram from a case of hypothyroidism showing sinus bradycardia, low voltage QRS, decreased amplitude of T wave and prominent U wave.

Figure 14. Diagrammatic representation of (A) normal electrocardiogram and (B) electrocardiographic findings in type 3 inherited long QT syndrome showing prolonged QT interval, late onset of T wave and prominent U wave.

Figure 15. Diagrammatic representation of inverted U wave on posterior surface of heart (leads V5, V6) producing reciprocal prominent U wave in anterior precordial leads (V4, V3).
Figure 19. Electrocardiogram showing U wave inversion in the sinus beat following a premature ventricular contraction (PVC).

Figure 20. Electrocardiogram from a patient of systemic hypertension showing U wave inversion in leads V3 to V6.

Figure 21. Electrocardiogram from a patient of systemic hypertension showing inverted U wave in leads V3 to V6.

It is characterized by prolonged QTc interval, late onset T wave and frequent prominent U wave (Figure 14).

(8) Significant narrowing of left circumflex or right coronary artery
It clinical context of myocardial ischemia, prominent U wave in precordial leads may suggest significant narrowing of left circumflex or right coronary artery. Exact mechanism is not known. It could be reciprocal to inversion of U wave on posterior surface of heart (Figure 15).

(9) Right ventricular compression
Yamagata et al have described new appearance of abnormal U wave in leads V1 to V3 following reconstructed stomach tube after surgery for cancer esophagus. Plain chest CT and transthoracic echocardiography demonstrated compression of right ventricular outflow tract and right ventricular free wall. Exact mechanism of new appearance of such abnormal U wave in this setting is not clear. Mechanical compression of heart has been reported to produce ECG changes similar to Brugada syndrome.7,8

(D) INVERTED U WAVE
U wave is normally inverted in lead aVR and sometimes in leads III, aVF and V1, if T wave is inverted in these leads. Inversion in other leads is abnormal.

(1) Inversion in left precordial leads (V3 to V6)
It can occur in following conditions.
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Figure 22. (A) Electrocardiogram from a patient of systemic hypertension with hypokalemia showing prominent U wave in leads V2 to V6 (B) Electrocardiogram recorded after correction of hypokalemia showing normalization of U wave.

(a) Acute myocardial ischemia
It is a marker of significant stenosis of left anterior descending coronary artery or left main coronary artery.10,11,12
(i) During attack of angina
(ii) During coronary spasm (Prinzmetal’s angina/variant angina)13
(iii) During exercise testing U wave inversion may precede ST segment depression (Figure 16)
(iv) Acute anterior myocardial infarction. U wave inversion may precede other electrocardiographic changes (Figure 17, 18).
(v) Post extrasystolic (pause dependent) U wave inversion also suggest underlying coronary artery disease13 (Figure 19).

(b) Left ventricular hypertrophy
(i) Systemic hypertension (Figure 20, 21)
(ii) Aortic stenosis
(iii) Hypertrophic cardiomyopathy
Presence of prominent U wave in presence of electrocardiographic findings of left ventricular hypertrophy should lead to suspicion of underlying hypokalemia (Figure 22).

(c) Hyperthyroidism11
(2) Inversion in lead I and aVL
It suggests lateral ischemia. Concomitant prominent U wave in leads V1 to V5 (Figure 23) suggests the possibility of additional posterior ischemia.
(3) Inversion in right precordial leads (V1, V2)
Right ventricular hypertrophy11
(4) Inversion in inferior leads (II, III, aVF)
Inferior ischemia
(5) Broad negative TU complex
Negative TU complex with prolonged QT interval can be seen in setting of myocardial infarction (Figure 24, 25) or raised intracranial pressure (Figure 26). As a reciprocal change TU fusion

Figure 23. Electrocardiogram showing U wave inversion in leads I and aVL with prominent U wave in leads V1 to V6.
wave is positive in lead aVR, right sided chest leads (V3R to V5R) and posterior chest leads (V7 to V9).

REFERENCES
MCQs

‘U’ Wave

Q1. U wave is usually most clearly visible in leads (A) V3R to V6R (B) V2, V3, V4 (C) V7, V8, V9 (D) II, III, aVF

Q2. U wave is usually best seen at heart rate (A) <65/min (B) 80 to 100/min (C) 100 to 120/min (D) >120/min

Q3. U wave is frequently seen in (A) Children (B) Adults (C) Middle aged (D) Elderly

Q4. Amplitude of normal U wave is (A) <2mm (B) 2 to 4mm (C) 4 to 6mm (D) >6mm

Q5. Amplitude of normal U wave is (A) <25% of T wave (B) 30 to 40% of T wave (C) 40 to 50% of T wave (D) >50% of T wave

Q6. Amplitude of U wave (A) Increases with decreasing heart rate (B) Increases with increasing heart rate (C) Decreases with decreasing heart rate (D) Is not affected by heart rate

Q7. In bifid T wave (A) Two apices are less than 0.16 second apart (B) Two apices are more than 0.16 second apart (C) Second peak is less than one third of the amplitude of first peak (D) Amplitude of second peak is more than 50% of the amplitude of first peak

Q8. In fusion of T wave and U wave

Q9. Prominent U waves suggest (A) Hyperkalemia (B) Hyponatremia (C) Hypercalcemia (D) Hypomagnesemia

Q10. Hypokalemia produces (A) Tachycardia (B) ST depression (C) Tall T wave (D) Tall U wave

Q11. Prominent U waves are seen in (A) Hypokalemia (B) Hypomagnesemia (C) Hyperthyroidism (D) Hyperthermia

Q12. Amiodarone produces (A) Prominent U wave (B) Broad T-U fusion wave (C) Torsades de pointes (D) All

Q13. Broad T-U fusion waves are produced by (A) Amiodarone (B) Dofetilide (C) Increased intracranial pressure (D) Thyrotoxicosis

Q14. Inherited long QT syndrome type 3 is characterized by (A) Prolonged QT interval (B) Early onset T wave (C) Prominent U wave (D) Inverted U wave

Q15. In context of myocardial ischemia prominent U wave in precordial leads (V5, V6) may suggest significant narrowing of (A) Left anterior descending coronary artery (B) Ramus artery (C) Left circumflex artery (D) Right coronary artery

Q16. U wave is normally inverted in lead (A) III (B) aVR (C) V1 (D) V4R

Q17. U wave inversion in leads V3 to V6 suggests (A) Myocardial ischemia (B) Left ventricular hypertrophy (C) Hypothyroidism (D) Hypermegnesia

Q18. U wave inversion in leads V3 to V5 suggests significant stenosis of (A) Left main coronary artery (B) Left anterior descending coronary artery (C) Left circumflex coronary artery (D) Posterior descending coronary artery

Q19. U wave inversion in leads II, III, aVF suggests significant stenosis of (A) Left main coronary artery (B) Left anterior descending coronary artery (C) Left circumflex coronary artery (D) Posterior descending coronary artery

Q20. U wave inversion in leads V1 and V2 can be seen in (A) Dilated cardiomyopathy (B) Myocarditis (C) Right ventricular ischemia (D) Right ventricular compression

Q21. U wave inversion can be seen in (A) Systemic hypertension (B) Aortic stenosis (C) Hypertrophic cardiomyopathy (D) Hypothyroidism

Poland Syndrome with Dextrocardia and Partial Agenesis of Ribs in Left Hemithorax

MONIKA MAHESHWARI

Poland syndrome is a rare congenital disorder, with incidence of 1:20,000 to 1:30,000 live births. It is characterized by ipsilateral absence of pectoralis major muscle. This syndrome is associated with various anomalies such as aplasia or hypoplasia of breast, ipsilateral syndactyly and brachydactyly, dextrocardia, herniation of lung etc. We report here, a rare case of Poland syndrome presented to us with dextrocardia with partial agenesis of ribs anteriorly beyond second rib in left hemithorax. These findings (dextrocardia associated with Poland syndrome without situs inversus nor complex intracardiac anomalies) confirm the hypothesis, that dextrocardia derives from a mechanical intrauterine displacement of a healthy heart toward the right side because of a lack of protection by the thoracic cage against external pressures.

Figure 1: Chest x-ray showing dextrocardia with partial agenesis of ribs anteriorly in left hemithorax, beyond second rib.
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T Wave
Flat T wave
Prominent (Tall) T waves
T Wave Inversion
QT Interval
'U' wave
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