超声心动图评价心脏再同步化治疗：操作及报告建议

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超声心动图在心衰病人的双心室起搏或心脏再同步化治疗(cardiac resynchronization therapy, CRT)中扮演着重要、而且不断演化的角色。近来有许多已发表的研究，应用超声心动图技术在CRT植入前辅助挑选适合CRT治疗的病人，在CRT植入术后协助优化起搏器参数设置，然而，仍未发现理想的方法。这份建议评估了当代超声心动图在CRT方面的应用，包括几种技术的相对优势和局限性，并对当前和未来可能的临床应用提出了建议。建议用于定性心室局部异常激活、即不同步(dyssynchrony)的首选方法应包括彩色组织多普勒测量纵向速度、常规脉冲多普勒测量左右室射血差异、或心室间机械延迟。补充测量径向收缩包括 M 型超声利用高质量的数据测量非缺血性心脏病患者的室间隔后壁延迟、或使用斑点追踪测量径向应变，都有附加的诊断价值。多普勒测量二尖瓣流入速度可作为CRT术后评价房室优化的简易指标。鉴于CRT是一个日新月异的领域，预计将来会不断有方法的修正和改进。

*关键词：*超声心动图，多普勒超声，充血性心力衰竭，起搏治疗

超声心动图在心衰病人的心脏再同步化治疗（cardiac resynchronization therapy, CRT）中扮演着很重要的角色。大量临床报导在植入CRT前使用超声心

动图来评价异常的机械运动，又称不同步(dyssynchrony)，从而有可能更好地选择适应症，或者指导起搏电极的植入部位。另外，超声心动图也被用于植入 CRT 后的参数优化设置。本共识的目的是评估当代超声心动图在 CRT 方面的应用，并对现在和将来可能的临床应用提出建议。该领域相对较新且发展较快，新信息不断涌现，目前并未界定最优方法，因此本共识对目前主要技术的优势和局限性进行讨论的同时，对临床实践也提出了建议。

再同步化治疗的临床益处

CRT 主要对于心衰、左室收缩功能障碍、机械不同步的治疗有效，而不同步收缩通常通过心电图异常心电激活识别。CRT 也称为双心室起搏(biventricular pacing)，已被数个随机临床试验证明可改善心力衰竭功能级别、运动耐量和生活质量，同时可减少住院时间和延长生存时间（表 1）[1-7]。另外，CRT 也可减少二尖瓣返流、改善左室功能 [2,8-12]。目前批准的 CRT 适应症包括纽约心脏病协会（NYHA）分级心功能 III 或 IV 级、QRS 波增宽≥120 毫秒、以及左室射血分数（LVEF）≤35%的严重心衰病人 [13]。尽管随机临床试验显示疗效很好，但大约仍然有 25%—35%接受 CRT 治疗的病人效果并不理想。超声心动图和多普勒成像技术在 CRT 病人的治疗中有着潜在的应用价值。尽管 CRT 治疗无反应有几个可能的原因，但是心电图 QRS 增宽不是心脏不同步的最佳的标志，而超声心动图量化不同步可能更好地选择 CRT 适应征 [12,14-16]。PROSPECT 研究（预测对 CRT 的反应）是近期的一项包括欧洲、美国和香港的多中心研究 [17,18]。虽然这项研究的最终结果还未得出，但是初步结果表明超声技术因素复杂，影响对不同步的分析，超声实验室的培训和专业知识对结果的可靠性非常重要。PROSPECT 研究也提示有些与分析差异相关的技术问题尚未解决，需要更多的工作来提高不同步分析的可重复性。

机械不同步概述

正常心脏的心电激活通常发生在 40 毫秒内，通过浦肯野系统传导，并与心脏各区域的同步机械收缩耦联。许多心肌病病变可引起心脏结构及功能改变，进而导致不同心脏区域的收缩发生提前或延迟，即产生不同步 [19]。虽然有些学者也

用“asynchrony”这个名词，我们在本文中用“dyssynchrony”来描述这一现象。尽管部分心衰或左室功能下降伴窄 QRS 波的病人中也可出现机械不同步，但是不同步通常与心电图 QRS 波时限延长有关，[20,21]。鉴于目前 CRT 临床实践中多用于 QRS 波群增宽的病人，本文以 QRS 波增宽的病人为重点。　　心肌不同步可分为三种类型：心室内(intraventricular)、心室间(interventricular)、房室间(atrioventricular)。左室不同节段机械收缩时间的异常，称为心室内不同步，似乎与收缩功能障碍最为相关，并可受 CRT 影响。因此多数超声多普勒参数以心室内不同步为主，我们在本文中除非特别注明，用“不同步”来指代“心室内不同步”。经典的心室收缩不同步源于异常心电激活，见于左束支传导阻滞。左束支传导阻滞表现为室间隔提前激活，而左室后壁、侧壁较晚激活[19]。室间隔在正常射血之前收缩，这时左室压力较低，该收缩无助于左室射血。该过程中一侧心室壁收缩，对对侧壁产生压力，在左室中产生不均匀的压力(stress)和应变(strain)，通常室间隔收缩早，引起后外侧壁拉伸或变薄，随后后外侧壁收缩晚，引起室间隔拉伸或变薄[22]。不同步导致左室收缩效率降低，舒张末容积和室壁压力升高，并导致舒张延迟，而舒张延迟被认为可影响参与调节灌注和基因表达的生物信号转导过程[23]。左室收缩同步化可改善左室功能，减少二尖瓣返流[8,24-28]。

量化机械不同步的常用方法

由于大多数 QRS 增宽的病人有机械不同步，影像检查的一个重要目的是通过识别 QRS 增宽而没有机械不同步的少部分患者，从而更好的选择适于 CRT 治疗的患者。出现这种情况的病理生理原因尚不清楚，不同步不明显甚至没有不同步的患者对于 CRT 治疗有反应的机率较小，而且 CRT 治疗后仍然预后不良[15]。也有其它原因导致对 CRT 治疗无反应，包括缺血性疾病致心肌疤痕过多以至于无法重构、CRT 治疗后发生梗死、导线位置不够好、以及其他未明原因[24,29-33]。没有不同步只是对 CRT 治疗无反应的一个因素，但它是一个可以通过多普勒超声心动图在 CRT 前识别的因素。

PROSPECT 研究表明，不同多普勒超声心动图方法的可行性和可重复性，可影响多中心研究的结果[17-18]。一些心衰病人的机械不同步的量化比较复杂，目前

没有单一的理想方法。然而，目前建议综合多个指标来帮助判断一个患者是否存在明显的不同步收缩，如果用不同方法分析得出模棱两可的结果，则需具体情况具体分析。常规二维超声心动图作为首选检查是很合理的。训练有素的检查者经常能目测评估典型左束支传导阻滞的收缩不同步，表现为室间隔早期一进一出运动，又称为室间隔闪现或反弹。严重心衰的病人是否有不同步收缩的存在或缺失可能比较细微，目测评估方法不应独立使用，提倡使用多普勒超声心动图方法定量。

M 型超声

最简单的量化左室收缩不同步的方法是用传统的 M 型超声心动图来记录室间隔-后壁运动延迟（septal-to-posterior wall-motion delay）（图 1A）。

步骤 1：选择胸骨旁左室长轴或左室短轴切面。

步骤 2：将 M 型超声的取样线放在左室中段水平（乳头肌水平）。

步骤 3：调节扫查速度为 50-100 毫米 / 秒。

步骤 4：测定室间隔向内收缩运动的最高点和后壁向内收缩的最高点之间的时间间隔。

Pitzalis 等报导在一组样本量为 20 人的非缺血性心肌病患者的实验中，以室间隔后壁延迟大于或等于 130 毫秒作为左室不同步的标志，其预测左室收缩末容积指数减少 15%或以上并有临床预后改善的敏感性为 100%，特异性为 63%[34-35]。室间隔后壁延迟越长，CRT 后左室逆重构程度越明显。许多病人由于室间隔运动复杂，涉及室间隔和后壁的主动运动和被动运动异常，因此室间隔后壁延迟的测量可能较为困难。Marcus 等在 CONTAK-CD 试验中入选了 79 例病人，他们的 M 超数据分析也体现了这一局限性[36]。他们发现 M 超测量结果的重复性不甚满意，CRT 有反应者（定义为左室收缩末容积减少 15%或以上）与无反应者的室间隔后壁延迟相近。PROSPECT 研究也发现数据分析的变异程度较大[17-18]。因此，不推荐 M 超独立用于不同步的定量，但可考虑作为其他方法如组织多普勒（tissue Doppler, TD）的补充，特别是 M 超在缺血性心脏病患者中的实用性还未被证实。

彩色组织多普勒（color TD）M 型超声

彩色组织多普勒 M 型超声是 M 超测量左室不同步的有益补充（图 1B）。通过对运动方向的改变进行彩色编码，可帮助识别室间隔和后壁从向内收缩向外舒张的转变。彩色组织多普勒 M 型超声测量室间隔后壁延迟≥130 毫秒被认为是有意义的不同步，但彩色组织多普勒 M 型超声也有与上述 M 超相似的局限性。

组织多普勒纵向速度（longitudinal TD velocity）

大部分文献用组织多普勒测量心尖切面左室纵向缩短速度来定量不同步[14-16, 37-49]。这是目前临床使用的主要方法，该方法的局限性下文将讨论。有两种基本方法：彩色编码组织多普勒和脉冲组织多普勒。

彩色组织多普勒数据的获取

彩色组织多普勒数据的获取比脉冲组织多普勒更简单实用，若超声仪器能够采集高频彩色组织多普勒，本委员会一致同意推荐该方法。几个主要的仪器供应商目前的硬件、软件设备可使高频彩色组织多普勒的帧频高于 90 帧/秒。不同的超声系统其彩色组织多普勒可能存在差异，但是细节仍未被阐明。

步骤 1：调节心电图至无噪音状态，QRS 波形清晰。

步骤 2：优化二维成像，以确保最大的心尖至近场左房成像，调节总增益和时间增益使心肌清晰显示。

步骤 3：将左室腔显示在扇形区中心并尽量垂直，使多普勒取样角度与左室纵向运动达到优化。

步骤 4：将深度设置为包括二尖瓣环水平。

步骤 5：启动彩色组织多普勒，调节使彩色组织多普勒涵盖整个左室，并以实现高帧频为目标（通常大于 90 帧/秒）。必要时减少深度及扇区宽度、聚焦在左室以提高帧频。调节总彩色增益使心肌清晰显示。若条件允许，速度达峰时间（time to peak velocity）可以用彩色编码在线显示。

步骤 6：让患者屏住呼吸。因为低速组织多普勒数据易受呼吸运动影响，我们推荐让病人短暂屏住呼吸，采集 3-5 个心动周期，通常采用呼气末时相，但也

可以采用图像质量最清晰的时相。若患者有房性或室性早搏，采集的心动周期数要相应增加。

步骤 7：记录三个标准切面：心尖四腔心、心尖两腔心、心尖长轴。

步骤 8：确定左室射血间期（LV ejectional interval）。通常在心尖五腔心或心尖长轴切面通过脉冲多普勒记录左室流出道血流来测定（图 2）。

彩色组织多普勒数据分析

彩色组织多普勒的最大优势是可以离线分析时间-速度数据。不同的超声仪器供应商具体的分析方法亦不同，但大体步骤相似：

步骤 1：确定左室射血间期，通常以脉冲频谱多普勒显示左室流出道血流的始末。所使用的超声系统不用，具体细节亦不同，但通常以心电图作为计时器。计算射血开始至射血结束的时间作为射血间期用于随后的时间-速度曲线分析。

步骤 2：在左室壁基底段、中间段的相对的两侧（每个切面有 4 个区域）选择感兴趣区的位置并确定感兴趣区的大小（最小为 5×10mm 至 7×15mm），获得时间-速度曲线。

步骤 3：可能的话，明确速度曲线的各部分组成，检查生理信号的质量，包括等容收缩速度（通常自 QRS 开始 60 毫秒以内）、朝向探头的收缩波或 S 波、以及背离探头的舒张早期 E 波和舒张晚期 A 波（图 3 和图 4）。

步骤 4：人工调节将感兴趣区纵向置于相邻的左室壁，识别射血期间峰值速度重复性最好的位点，这是寻找最高峰值的重要步骤，特别是在有多个峰值或存在信号干扰的情况下。如果在射血间期对于感兴趣区的微调未能产生单一可重复的峰值，则选择较两个或更多的同样峰值中较早的那个峰值。

步骤 5：判断每个区域从 QRS 波群起点至达到收缩期峰值速度的时间：每个切面 4 个节段，每例病人 3 个切面，一共 12 个节段。另一种替代方法是测定对侧壁 S 峰峰值时间的差异，即下文中将描述的对侧室壁延迟法（opposing wall delay method）。这种方法较简单，即同一帧影像中某个室壁的 S 峰到对侧壁的 S 峰的时间差，不需测量 QRS 波起点。

步骤 6：由于每次心动周期可能存在差异，计算所采集的不同心动周期中的速度达峰时间并取平均值，可以提高可重复性。建议最少取 3-5 个心动周期的平

均值，如果每次心跳确有差异，则需取更多个心动周期的平均值，并排除房性早搏或室性早搏相关的数据。房颤病人的组织多普勒数据分析更为复杂，目前没有数据支持合并房颤时的不同步分析。

收缩晚期速度 （postsystolic shortening velocity）

一些先前研究分析了收缩晚期的不同步缩短（主动脉瓣关闭后心肌的正向速度，峰值可能比射血间期峰值更高）[47]。用主动脉瓣开放到主动脉瓣关闭期间的纵向峰速作不同步分析对预测 CRT 治疗反应的敏感性和特异性更好 [34,43]。Notabartolo 等[47]测量了包括基底部 6 个节段在内的收缩晚期速度达峰时间的最大差异，以大于 110 毫秒预测左室逆重构，其敏感性高达 97%，而特异性降至 55%。所以虽然最优的方法仍未完全阐明，目前大多数证据仍支持射血间期峰值速度分析是较好的方法。

应用彩色组织多普勒的临床研究

很多研究都是采用彩色组织多普勒评估左室收缩不同步，以及预测预后，这也是本写作组目前认可的方法。最简单的评估左室不同步的彩色组织多普勒方法，是在心尖四腔心切面的左室基底段测量室间隔间隔侧壁延迟，称为两点法[15]。也可以用包括四个基底段（室间隔、后壁、下壁、前壁）的四节段模型。 对侧室壁延迟（opposing wall delay）大于或等于 65 毫秒，可以预测 CRT 的临床反应（纽约心功能分级和 6 分钟步行距离评估）以及逆重构（左室收缩末缩容积缩小大于 15%）[15]。另外，大于或等于 65 毫秒的左室不同步的病人植入 CRT 后疗效更明显 [15,48]。对侧室壁延迟的方法还可以扩展到三个标准的心尖切面：四腔心、两腔心和左室长轴，在心尖三个切面中的每个切面四点测量速度达峰时间的最大差异，定义为最大对侧室壁延迟。三个切面模型最重要的特征是，它包括了心尖长轴切面的前间隔和后壁，而这两个节段的不同步很常见[3]。Yu 等人建立了十二节段标准差模型（12-segment SD model），整合三个心尖切面（四腔心、两腔心和左室长轴）的彩色多普勒数据[31,43]。机械不同步指数（mechanical dyssynchrony index）也称 Yu 指数（Yu index），通过计算射血间期十二节段的速度达峰时间的标准差得到 [31,43,49]。通过参考健康人群中的测量，十二节段标准差大于或等于

33 毫秒为机械不同步，用于 QRS 波大于 150 毫秒的病人时，可预测左室逆重构（收缩末容积减小大于或等于 15%）的敏感性 100%，特异性为 78%。对于 QRS 波介于 120 毫秒和 150 毫秒的患者，其敏感性为 83%,特异性为 86%[49]。另一种方法计算所有节段速度达峰时间的最长时间差，大于或等于 100 毫秒预示 CRT 有良好反应[31,43]。PROSPECT 研究显示十二节段速度达峰时间标准差与其他它简单方式相比，成功率较低，变异性较大，缺点是技术要求更高[18]。

组织多普勒另一延伸技术是自动彩色编码速度达峰时间的数据，其中一个就是组织同步化显像（tissue synchronization imaging, TSI）（图 5）。将组织同步化显像的数据重叠添加在二维超声图像上，用于视觉识别机械收缩延迟的节段，主要应当看射血间期，避免等容收缩期和收缩晚期。Gorcsan 等采用 组织同步化显像彩色编码指导放置感兴趣区，发现前间隔-后壁延迟大于或等于 65 毫秒，可以预测植入 CRT 后每搏输出量的快速改善[12]。

Yu 等也采用 TSI 观察了 56 例患者，发现十二节段的组织同步化显像 计算所得的达峰时间标准差（Ts-SD）的受试者操作特征曲线（receiver operating characteristic curve）面积最高，为 0.9，包含收缩晚期数据能明显减少操作特征曲线面积至 0.69。而且，与直接由时间速度曲线得到的数据相比，所有组织同步化显像得到的参数，其预测价值均稍有降低[50]。因此，应用组织同步化显像技术时，建议调整感兴趣区，检查心肌的时间速度曲线，以确保组织同步化显像所显示的峰速度的准确性。

脉冲组织多普勒（pulsed TD）

脉冲组织多普勒可用于评价左室不同步，而且大部分心脏超声系统都可以测定（图 6）。脉冲组织多普勒的预设必须由各自的生产商优化。一般是参考上文所述的彩色组织多普勒数据采集和分析的步骤，并有些改变。脉冲多普勒采样将容积设定为大约 1 厘米的长度，速度范围设定应当使时间速度曲线最大化，扫描速度设置为 50 到 100 毫米/秒。与离线彩色组织多普勒数据分析不同，采样容积在段内移动寻找可重复的时间速度信号必须在线完成，这是脉冲组织多普勒的最大劣势，比较耗时而且容易受呼吸、病人移动以及心率变化的影响。另外，射血

间期必须人工确定，并且心脏收缩速度的频谱形态较宽，有平台期，峰值速度可能很难确定。鉴于这些技术上的限制，彩色组织多普勒更被本写作组认可。目前，关于脉冲组织多普勒预测 CRT 反应的临床研究比彩色组织多普勒的研究少。Penicka 等人应用脉冲组织波多普勒测定心尖四腔心、左室长轴的各基底段和右室侧壁的收缩起始时间[51]，应用心室间以及心室内不同步超过 100 毫秒的综和指数，识别了除 6 个以外的所有 CRT 有效的病人，准确率为 88%。

组织多普勒纵向应变（longitudinal strain）、应变率(strain rate)以及位移(displacement)

应变和应变率成像理论上的优势在于能区分出心肌主动收缩和被动牵拉变形，已被用于识别心室运动的不同步[40,42,52]。纵向应变由组织多普勒速度信号计算出心肌缩短率（图 7），然而组织多普勒纵向应变技术挑战在于应变由沿着取样线的数据计算，受多普勒角度限制，严重心力衰竭患者左室多呈球形改变，加大了技术难度。Breithardt 等人通过比较心肌速度和应变率，发现心肌节段运动（速度参数）与变形（应变率图像参数）相关[52]，并得出结论，心肌时间速度数据不能完全反映心脏不同步的程度，特别是在缺血性心肌病病人中，心肌变形应该是评价同步性的推荐方法。Sogaard 等人发现，基底段纵向收缩的延迟程度能预测植入 CRT 后左室 EF 的改善程度[41,42]。然而，Yu 等人发现应变率参数显像数据不能预测左室逆重构[43,44,53]。目前，组织多普勒应变率受信号噪声比的影响，限制了它的可重复性。另一方面，应变分析的改进，包括利用常规灰阶图进行斑点追踪（speckling tracking）测定应变的软件，对评价收缩同步性很有应用前景[54]。

位移成像（displacement imaging）利用组织多普勒数据来计算心肌运动的距离，通常经彩色编码后叠加在二维图像上。虽然它的信号-噪声比与应变及应变率成像相比更有优势，但是位移成像也会受被动运动及多普勒角度的影响。有研究显示位移或组织跟踪指标在植入 CRT 后有所改善，但是其预测疗效和临床预后的参考值尚未建立[42]。

径向应变（radial strain）

径向增厚是左室收缩的主要构成部分之一，短轴动力学是评价心脏不同步的重要参数[55]，因此在全面检查中应用这个指标是很合理的。与M型超声相比，应变能区分主动和被动运动，并确定径向机械活动[56]。Dohi 等人首次应用组织多普勒应变来量化38例植入CRT病人的径向机械不同步[57]。径向应变由左室短轴中段切面前间隔与后壁的组织多普勒速度计算得出[58]。组织多普勒径向应变的缺点是如果成像质量不够好，则信号噪音较大，而且受多普勒角度的影响。

最近应用的斑点追踪技术，可以利用常规灰阶超声心动图进行分析，不受限于多普勒角度。Suffoletto 等人应用这种方法法研究了64例植入CRT的病人。左室中段短轴切面应用斑点追踪于获取并计算六个标准节段内不同点的径向应变平均值（图8）[54]。其中50例病人随访8±5个月，基线斑点追踪计算的径向不同步（室间隔与后壁应变峰值延迟时间大于或等于130毫秒）、可以预测左室射血分数能有明显的改善敏感性为89%，特异性为83%。一个有趣的亚组病人是纵向组织组织多普勒速度并未发现不同步，而斑点追踪显示径向不同步，对植入CRT也有良好疗效。这些数据表明，短轴切面评价不同步是对长轴切面的有益补充。最近的一项研究对176例病人进行组织多普勒显像测量心肌纵向速度和斑点追踪技术测量径向应变，发现纵向和径向皆不同步的患者植入CRT后改善射血分数的机率比较高[59]，而纵向或者径向皆同步的患者则改善射血分数的机率较低。这些数据表明，两者联合预测对CRT的反应优于单一技术[59]。

三维超声心动图

左室不同步实际上是一个三维现象。三维超声心动图技术是评价左室机械不同步独特而有效的工具[60]。三维超声心动图优点是可以在同一心动周期中评价左室各个节段的整体机械不同步情况（图 9）。应用半自动轮廓追踪计算法，可将室壁节段运动可视化及量化。初步研究显示，这种方法通过直接比较左室所有节段心内膜侧的室壁运动，可以全面分析植入 CRT 前后左室室壁运动的变化。。Kapetanakis 等人应用左室所有的十六个心肌节段达到收缩期末最小容积的时间离散度计算得到26例植入CRT患者的收缩不同步指数，发现该收缩不同步指数可以预测左室逆重构[61]。三维超声心动图技术为更全面分析左室不同步提供了有效评价方法[62]。然而，它的不足之处包括较低的空间、时间分辨率和帧率，三

维广角采集的图像约为 20 到 30 帧/秒。

心室间不同步

心室间不同步，是指心室间机械收缩延迟（interventricular mechanical delay,IVMD），是左右室射血间期的时间间隔。通常由脉冲多普勒测量 QRS 波起点到左右心室流出道血流频谱起始时间的时间差，两者时间差大于 40 被认为心室间不同步（图 10）[63-65]。IVMD 作为心衰患者症状恶化、心源性死亡增高的指标，对判定 CRT 植入后的预后有价值（通常 IVMD 超过 40-50 毫米）[65]。尽管 IVMD 操作简单，重复性好，常用超声机器即可测量[15]，但似乎对预测 CRT 反应的特异性较差。Bax 等人研究发现，59 例对 CRT 有反应和 21 例无反应的病人，两者心室间不同步时间相似（47±34 vs 49±29ms，差异无统计学意义）[16]。Achilli 等人曾报道，133 例患者的 SCART 研究中，心室间不同步时间超过 44ms 的患者对 CRT 有良好的反应，敏感性 66%,特异性 55%[63]。Richardson 等人也研究表明，在 CARE-HF 研究中心室间不同步超过 50ms,对植入 CRT 后病人预后的判断有价值[65]。PROSPECT 临床试验显示，IVMD 和其它简单脉冲多普勒测量心脏不同步的方法，例如射血前期延迟（pre-ejection delay）、左室充盈时间与心脏周期比例，在多中心研究中能有较高可行性和高重复性[18]。然而，象很多研究左室内不同步一样，心室间不同步并不能有效预测植入 CRT 效果。表 2 为目前测量心脏不同步的主要方法。

评估心脏不同步的其它方法

Breithardt 等人报道了一种用半自动方法描绘心内膜来进行相差分析的方法[66]。选取常规心尖四腔心二维超声心动图，重点分析室间隔侧壁的同步性来定量评价左室不同步的程度。超声系统自动生成室壁各节段的运动曲线，再根据傅里叶转换进行数学相差分析计算室间隔侧壁相位差,即为心室内不同步的定量评价指标。另一种应用常规超声评价不同步的方法是速度向量成像（velocity vector imaging）。这种方法通过一系列独特的 B 型超声像素追踪（B-mode pixel tracking）计算局部心肌相对操作者选定点的运动速度（图 11）。Cannesson 等人的一项预实验，追踪了 23 例 CRT 植入患者，应用单心动周期标准心尖切面电

影回放测定左室壁中段运动[67]。标准心尖三个切面中对侧室壁径向收缩速度达峰时间延迟超过或等于 75 毫秒即被定义为不同步，对预测 CRT 植入后随访 8±5 个月射血分数的变化的敏感度为 85%、特异度为 80%。

对左室逆重构和二尖瓣返流的影响

左室重构是心室不断扩张、心腔形态变形、二尖瓣几何形态变形并伴随瓣膜返流增多以及心室收缩功能不断恶化的动态过程，最终导致心衰[68,69]。左室重构可能由压力或容量负荷过重、或者由心肌缺血损伤导致心肌细胞减少而触发，或者由基因异常导致[70]。尽管左室重构的确切机制和信号传递途径不明确，但是神经内分泌和局部促心肌肥大因子可以调控心室扩张和细胞外基质限制扩张的平衡，进而影响心肌功能基因的表达[23]。CRT 植入后随着时间推移，往往对左室大小和功能改善起到逆重构的作用。左室逆重构具有 CRT 依赖性，终止 CRT 治疗会导致左室功能进行性恶化，并回到基线水平。 MIRACLE 和其它一些临床试验显示，不同原因所致的心衰左室逆重构的程度也不一样。虽然非缺血性心肌病人左心室更大、射血分数更低，但是左室容积与二尖瓣返流程度的减少、射血分数的增加，在非缺血性心脏病患者中的改善程度是缺血性心肌病患者的 2-3 倍[68]。一项研究对植入 CRT 治疗的 141 例患者进行随访发现，3-6 个月内左室收缩末容积减少 10%以上的患者，有更明显的远期临床效果，包括更低的全因死亡率（7% vs 31%），、心血管死亡率（2% vs 24%）和心衰事件（12% vs 33%，P<0.05）[68,71]。

CRT 通过激活乳头肌协调机械活动，植入后早期很快减少二尖瓣返流，长期可以通过促进逆重构改善左室大小和几何形状（图 12）[28]。 Breithardt 等人应用近端等速度表面积（proximal isovelocity surface area, PISA）法发现，植入 CRT 一周后 CRT 开启与 CRT 关闭比较，能明显减少反流容积，从 32±19ml 减少到 19±9ml；也能有效地减少有效反流口面积，从 25±19 mm2 减少到 13±8mm2[8]。一个二尖瓣反流面积快速减少的重要原因是植入 CRT 后，两侧乳头肌的协调性增加，从而增加二尖瓣对合面积。Kanzaki 等人应用机械应变激活成像（mechanical strain activation mapping）的方法显示，二尖瓣反流的减少与 CRT 植入后早期协调乳头肌机械收缩的激活时间 有关[28]。

起搏电极的放置

一些研究指出，通过超声心动图确认最晚机械收缩位置，对指导起搏电极植入具有潜在应用价值。Ansalone 等人也首次发现组织多普勒超声测定收缩速度，在收缩最晚的部位植入电极，可提高 CRT 疗效[30]。他们发现 75%病人的最晚激动部位在左室下壁和后侧壁。Murphy 等人也证明利用彩色编码速度达峰时间确定机械运动最晚的部位， 可以提高 CRT 临床疗效和血流动力学获益[72]。随着 CRT 植入位点的不同，左室呈阶梯式的反应，植入 CRT 患者平均随访 6 个月后，如果电极植入位点距离最大延迟位点相差一个节段，则起到弱或者相对有限的逆重构作用；如果电极植入位点距离最大延迟位点超过一个节段，CRT 则没有明显逆重构的作用。

Suffoletto 等[54]在 CRT 治疗前，应用二维斑点追踪技术分析左室径向应变，寻找患者最大机械延迟位点，将左心室起搏电极植入至最晚激动的位点，可促进左心室发生逆向重构。研究发现，与 24 例起搏电极植入非恰当位置患者相比，起搏电极植入至最晚激动位点的 22 例患者左室射血分数（10±5%）有更明显的改善作用（6±5%，P<0.05），虽然这些研究鼓舞人心，但超声心动图在指导左室电极植入中的作用仍需要前瞻性研究来确定。

AV 间期优化的基本原理

心室植入 CRT 后，AV 间期需要程控调整。起搏治疗理想的 AV 间期是在左心室收缩之前，完成心室舒张期的左房收缩，优化左心室收缩前负荷[73]。如果 AV 间期太短，则心室收缩提前，二尖瓣提前关闭，心房收缩（二尖瓣Ａ峰）被迫过早终止。如果 AV 期间太长，可能出现舒张期二尖瓣反流和左心室收缩前负荷低，甚至导致左心室未被起搏前即去极化，不能达到 CRT 左心室起搏的目的。

尽管房室同步化在 CRT 患者中的重要性勿庸置疑，但是否所有的 CRT 患者均需要常规多普勒超声心动图优化 AV 间期是有争议的，因为到目前为止还没有一个标准可靠的方法，而且需要超声心动图与心脏电生理技术人员协同工作，时间安排上也会有一定的困难。Auricchio 等人认为，尽管 AV 间期对心脏血流动力学影响很大，但左心室的同步性比 AV 间期更重要[74]。目前，许多中心 CRT 植入后 AV 间期使用出厂设定的经验值，大约为 100-130 毫秒，还有些研究中心依据心

电图 QRS 波及 PR 间期的时限参数去优化最佳 AV 间期,,如果 QRS 波时限大于 150 毫秒，则最优 AV 间期为 PR 间期时限(毫秒)×0.50,如果 QRS 波时限小于 150 毫秒，则最优 AV 间期为 PR 间期时限(毫秒)×0.70[75]。Sawhney 等学者最近对 40 例 CRT 植入患者进行了一项前瞻性随机试验,比较了经多普勒超声优化的 AV 间期和 AV 间期为 120 毫秒[76]。在 CRT 植入后 3 个月，优化组病人 NYHA 心功能分级和生活质量有改善,但 6 分钟步行距离或左室射血分数没有显著改善。在一个更大的有 215 名患者参与的研究表明，多普勒超声心动图 AV 间期优化程控之前和之后 AV 间期差别不大(分别为 120 毫秒和 135 毫秒)，与没有接受 AV 间期优化之前有微小的差异变化[77]。此外，只在少数的 CRT 患者身上，在 AV 间期优化后，左心室血流动力学得到改善,表明很大一部分的病人不需要正式的 AV 间期优化。在未经多普勒超声心动图优化前，有心房内传导延迟的患者对优化后 AV 间期达到 150250 毫秒时，受益最大（图 13）[77]。这部分患者二尖瓣口血流频谱 A 峰消失，AAV 间期的经验设置对这部分患者来说太短。虽然对 CRT 植入后 AV 间期优化还没有明确的建议，但是下文中内容可供参考。

Ritter 法和递减重复法优化 AV 间期

Ritter 法和递减重复法利用二尖瓣口血流脉冲多普勒频谱评估左心室充盈,利用左室流出道前向血流的脉冲多普勒频谱或连续多普勒频谱评估左室射血能力[78、79]。Ritter 等试图通过使心房收缩的结束时间和心室收缩的起始时间同步[79]，需要设定一个短 AV 间期(50 毫秒),然后设定一个长 AV 间期(200 或 250 毫秒)，测试对舒张充盈的影响，然后用短和长 AV 间期的心房收缩后心室收缩起始时间的差值，来校正长 AV 间期。。递减重复法更简单,将 CRT 程控为心房同步的心室起搏，一般从 AV 间期 200 毫秒开始,以 20 毫秒递减，直到 AV 间期为 60 毫秒，检测一系列 AV 间期，最佳的 AV 间期是二尖瓣血流频谱 E 峰和 A 峰分离、且 A 峰频谱在心电图 QRS 波起始前 40-60 毫秒终止对应的 AV 间期，通常呈舒张功能异常 I 期（松弛异常）的频谱[80]。技术要领包括将脉冲多普勒的取样容积放置在更靠近心房的二尖瓣瓣叶关闭对合线的位置（而不是置于二尖瓣尖的标准位置），以更好地检测到二尖瓣的闭合；用较高的扫查速度和低滤过；如果可能的话，将 CRT 的心电信号直接导入超声系统。递减重复法还可以用主动脉瓣口血流速度来

反映每搏输出量。一般选择 AV 间期为 60 毫秒、80 毫秒、100 毫秒、120 毫秒、140 毫秒、和 160 毫秒，测定六个不同的 AV 间期主动脉瓣口血流时间速度积分，最大的时间速度积分相对应的是最佳 AV 间期。,每个设定之间，需要至少间隔 10 到 15 个心动周期。

简化多普勒超声筛查方法

由于目前尚无 CRT 植入后进行常规 AV 间期优化的共识，我们提出了一个简化的利用二尖瓣多普勒血流的筛查方法[77,81]（图 14）。

步骤 1:优化心电图信号,包括必要时反转 QRS 波群。

步骤 2:二尖瓣口血流流入速度使用高扫描速度、低过滤的脉冲多普勒测定,取样容积设定在二尖瓣瓣叶关闭线上。

步骤 3:检查二尖瓣口血流频谱，如果符合一下条件则不需要再进行 AV 间隔优化：

a. 可以清楚识别二尖瓣口血流 E 峰和 A 峰是分离的。 b.二尖瓣口血流频谱 A 峰在心电图 QRS 波前、或者二尖瓣关闭前至少 40 毫秒。

需要注意的是,超声多普勒显示的二尖瓣关闭作为左心室收缩起始的标志，应该与的 QRS 波同步。如果 CRT 术后二尖瓣血流频谱呈 E/A 倒置的舒张功能 I 期（松弛）的表现，改变 AV 间期没有改善作用，Kedia 等人建议，对于这部分患者，不需要进行 AV 间期优化[77]。如符合以下情况则建议进行 AV 间期优化：A 峰无法识别,E 峰和 A 峰融合,或者由于二尖瓣提前关闭引起 A 峰停止。如果二尖瓣血流频谱呈舒张功能不全 II 期(假性正常化)或 III 期(限制性充盈异常)，则应当考虑优化[77、80]。A 峰缺失可能与心房内传导延迟相关,通常需要更长的 AV 间期。但是如果 AV 间期设置太长,也可导致 E 峰和 A 峰融合。A 峰提前终止需要延长 AV 间期。对于以上的情况，究竟是选择递减重复法，还是 Ritter 法来完成 AV 间期优化，往往取决于操作人员的偏好。房颤、频发室早或心动过速患者不适合进行 AV 间期优化。二尖瓣人工心脏瓣膜置换术后的患者也无法用本方法进行 AV 间期的优化。

双心室优化

最近一代 CRT 起搏装置可以优化双心室之间的延迟(V-V delays)[82-86]。Sogaard 等人首次报道了 CRT 人群 V-V 优化获益的证据[87]。该报道对 20 例 CRT 患者进行V-V优化,发现可以使左室射血分数进一步改善,(CRT植入前为22±6%,CRT 植入后增加至 30±5%，V-V 优化后进一步增加至 34±6% ,P<0.01)。此外,Bordachar 等证明 V-V 优化可以令二尖瓣返流显著减少[88-89]。V-V 优化通常是通过改变 V-V 激动先后顺序进行，从左心室比右心室优先激动开始,然后逐步加长或缩短 V-V 间隔(例如,2 递减或递增 20 毫秒)，测量主动脉瓣血流最大的时间速度积分。

目前的研究表明,部分病人可以从 V-V 优化中取得明显的短期获益,但长期是否获益尚未确定。

窄 QRS 波患者的不同步

一部分窄 QRS 波（持续时间小于 120 毫秒)的心力衰竭患者也可能有机械不同步。如果可以证明 CRT 植入有利于该类心力衰竭患者,那么应用超声心动图评估机械不同步对选择 CRT 适应症非常重要[20,21,64]。Bleeker 等人报告了 33 例 NYHA 心功能 III 或 IV 级、LVEF≤35%、QRS 波时限小于 120 毫秒的心力衰竭的患者，组织多普勒显示室间隔侧壁收缩达峰时间延迟大于或等于 65 毫秒，存在机械不同步，他们在 CRT 治疗中获益。[90]。在另一项研究中,, Yuet 等人研究了 51 例窄 QRS 波(小于 120 毫秒)的心力衰竭患者，组织多普勒证实有不同步，CRT 可以减少左心室收缩末期容积,改善 NYHA 心功能分级,提高 6 分钟步行距离,并且增加 LVEF,这样的获益与宽 QRS 波的心力衰竭患者接受 CRT 的获益相似[91]。Beshai 等人最近发表了第一个窄 QRS 波(小于 130 毫秒)的心力衰竭患者 CRT 植入的随机试验,称为 RethinQ 试验[92]。该项研究中，收缩不同步定义为在心尖四腔心或心间长轴切面室间隔侧壁的收缩速度达峰时间差别大于等于 65 毫秒，或者 M 型超声分析室间隔＝后壁收缩达峰时间延迟大于等于 130 毫秒，所有符合标准的患者 96% 符合组织多普勒的入选标准的患者)均植入了 CRT,172 名入选者被随机分配为 CRT 功能启用或 CRT 功能关闭。该试验的主要终点是 CRT 后心肌耗氧量增加，CRT 未显示疗效，CRT 改善了次要终点即 NYHA 心功能评级恶化，但是对其它参数包括患者生活质量得分、6 分钟步行距离、以及左室逆重构没有变化。然而在非

缺血型心肌病患者疾病中，CRT 可以改善患者的 6 分钟步行距离。亚组分析也表明，对于那些 QRS 波时限为 120130 毫秒、并有不同步的患者，CRT 可以明显改善最大心肌耗氧量和改善 NYHA 心功能评级[92]。RethinQ 随机试验的总的结果是阴性的,但是仍然存在许多悬而未决的问题，目前尚不清楚是否应当界定窄 QRS 波心力衰竭人群中不同步的类型或程度，以预测对 CRT 是否有效。很明确的是，将需要更大规模的随机临床试验来验证 CRT 对窄 QRS 波心力衰竭的治疗作用，以及多普勒超声心动图在适应症选择中潜在的重要价值。

评估不同步在临床实践中的应用和超声报告

尽管上文讨论的一些超声心动图评估不同步的方法对于预测 CRT 疗效优于 QRS 波宽度，,但大规模临床试验和临床指南并没有应用多普勒超声心动图评价不同步来选择病人[13]。**因此,本写作组目前不建议已经符合公认 CRT 治疗指证的患者，因多普勒超声心动图分析不同步的结果而不植入 CRT。**

我们注意到,目前有许多中心运用这些分析辅助不完全符合 CRT 指证的病人进行 CRT 临床适应症的选择，如 QRS 波时限不完全符合标准。尽管临床试验在这方面数据有限,但是在 CARE-HF 随机 CRT 试验中入选标准中 QRS 时限为 120－149 毫秒,并满足以下 3 个评价不同步的条件之中的任意两个:主动脉射血前期时间延迟大 140 毫秒； IVMD 大于 40 毫秒;或左室后外侧壁延迟激活[6],[6]。此外,RethinQ 试验中 QRS 波 120 －129 毫秒且存在机械不同步的患者，可以获益于 CRT[92]。其它评价不同步可能可能有潜在应用价值的情况包括左室射血分数不完全符合标准、或 NYHA 心功能分类不清。如果临床上因以上情况需要进行超声心动图评价不同步，本写作组的共识是应行以下不同步的检测并出报告。

心尖四腔心或左室长轴切面对侧壁延迟(opposing wall delay，一侧室壁 S 峰与对侧室壁 S 峰的最长时间差)

机械不同步定义为对侧室壁的收缩达峰时间延迟≥65ms,或者 Yu 指数（十二节段标准差指数）≥33ms。

使用脉冲多普勒在右室流出道和左室流出道计算射血前期时间判断IVMD

左右心室射血间期前时间的差≥40ms 表示左右心室间存在机械收缩不同步。

径向运动分析有附加作用 ,包括在非缺血性心肌病患者中使用图像质量很高的 M-型超声，或者测量径向应变，来判断室间隔后壁机械延迟。

室间隔后壁收缩达峰延迟≥130ms 代表机械收缩不同步。

某些超声心动室报告中也可能包含表 2 的其它指标。因为最佳方法尚未明确,所以建议采取保守的方法来小心地排除机械不同步。如果不同方法结论一致，则不同步评估结果更为可信[59]。**我们建议超声报告中不应包括病人是否需要植入CRT，因为对于不完全符合 CRT 适应症，或是较疑难的病例，应当具体分析后作出临床判断，**本报告所描述的许多其它方法是有前景的,但目前技术上困难仍然很大或有待于进一步发展。

超声心动图在 CRT 患者的治疗中的作用很重要、而且不断变化,包括从定量分析心室功能的改善及二尖瓣返流的减少，到 CRT 植入后优化疗效。我们做了大量的研究工作来评估机械不同步，以更好地选择适合 CRT 的患者，并指导 CRT 电极在心脏的植入位置,但这是一个复杂且具有挑战性的工作,需要更多的研究，目前有几个很有前景的研究正在进行中。超声心动图数据采集和分析的改进,以及我们对机械不同步和 CRT 病理生理学的理解进一步加深,将在未来的临床实践和改善患者预后中有很好的前景。

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表 1 心脏再同步化治疗重要的临床试验总结

	MUSTIC	PATH-CHF	MIRACLE	MIRACLE-ICD
入选标准	NYHA III LVEF<35% EDD>60mm 6 分钟步行距离 <450 米 QRS=150ms	NYHA III-IV QRS>=120ms	NYHA III,IV LVEF<=35% EDD>=55mm QRS>=130ms	NYHA III,IV LVEF<=35% EDD>=55mm QRS>=130ms ICD 适应症
例数	58	40	453	369
观察终点	QOL，6 分钟步行试验，最大耗氧量，心衰住院率	急性血流动力学 QOL、6 分钟步行试验，心衰住院率	QOL，NHYA 评级，6 分钟步行试验	QOL，NHYA 评级，6 分钟步行试验
研究设计	单盲，随机，交叉	单盲，随机，交叉	双盲，随机，平行对照	双盲，随机，平行对照
治疗方法	CRT vs 无起搏	CRT vs 无起搏	CRT vs 无起搏	CRT vs ICD
主要发现	CRT 可以改善所有终点，降低住院率	CRT 可以改善急性血流动力学和慢性终点	CRT 可以改善所有终点，降低住院率	CRT 可以改善 QOL 和 NYHA 分级，不影响 ICD 功能

	CONTAK	COMPANION	CARE-HF
入选标准	NYHA II-IV LVEF<=35% QRS>=120ms ICD 适应症	NYHA II-IV LVEF<=35% QRS>=120ms	NYHA II-IV LVEF<=35% QRS>150ms 或 QRS=120-150ms 存在不同步
例数	333	1520	819
观察终点	死亡率，心衰住	主要终点：全因	全因死亡或非计

	院率，室速/室颤	死亡或住院率；次要终点：全因死亡	划住院
研究设计	双盲，随机，平行对照	随机，平行对照	随机，平行对照
治疗方法	CRT-D vs ICD	CRT vs CRT-D vs 无起搏	CRT vs 无起搏
主要发现	CRT 改善次要终点，主要终点无改善	CRT、CRT-D 改善主要终点，CRT-D 可以降低死亡率	CRT 改善主要终点，降低全因死亡率

CRT 心脏再同步化治疗；CRT-D 心脏再同步化+除颤治疗；EDD 左室舒张末内径；HF 心力衰竭；ICD 植入除颤器；LVEF 左室射血分数；NYHA 纽约心功能分级；QOL 生活质量评分；VF 室颤；VO2 最大耗氧量；VT，室速。

表 2 与心脏在同步化治疗反应有关的主要不同步指标

参数	方法	正常值	截点值	优点	缺点
心室内纵向不同步					
对侧壁延迟，两点法（12,15.38）	彩色组织多普勒峰值速度（心尖四腔心切面或长轴切面）	<50ms	≧65ms	操作快捷；可以线下分析	需要彩色组织多普勒软件；容易受到被动牵拉运动影响
最大室壁延迟，十二点（43,47）	彩色组织多普勒峰值速度（心尖四腔心切面、两腔心切面和长轴切面）	<90ms	≧100ms	可以更全面地分析纵向不同步；可以线下分析	需要彩色组织多普勒软件；容易受到被动牵拉运动影响
Yu 指数（14,31,43）	彩色组织多普勒，十二节段标准差（心尖四腔心切面、两腔心切面和	<30ms	≧33ms	可以更全面地分析纵向不同步；可以线下分析	需要彩色组织多普勒软件；费时；容易受到被动牵拉运动

	长轴切面）				影响
收缩起始时间延迟（51）	脉冲组织多普勒（心尖四腔心切面，两腔心切面和长轴切面；左室与右室）	<80ms	≧100ms	更多设备可测定	采集技术较难；不能线下分析；容易受到被动牵拉运动影响
纵向收缩延迟（41,42）	彩色组织多普勒应变，应变率（心尖切面）	无	N/A	不易受被动牵拉运动影响；可以线下分析	需要特殊的彩色组织多普勒软件；技术难度大
心室内径向不同步					
室间隔后壁延迟（34,35）	M 型（胸骨旁左室中段）	<50ms	≧130ms	容易测定；结果快；不需要特殊技术	很容易受到被动牵拉运动影响；局部室壁不运动时无法测量
室间隔后壁延迟（54,57）	径向应变（胸骨旁左室中段）	<40ms	≧130ms	不易受被动牵拉运动影响；斑点追踪可以用常规图像分析	需要特殊软件；只能分析径向动力学
心室间不同步					
心室间机械延迟（62-64）	常规脉冲多普勒（右室流出道和左室流出道）	<20ms	≧40ms	容易测定；无需复杂技术；可重复性好	非特异性；容易受左室、右室功能影响

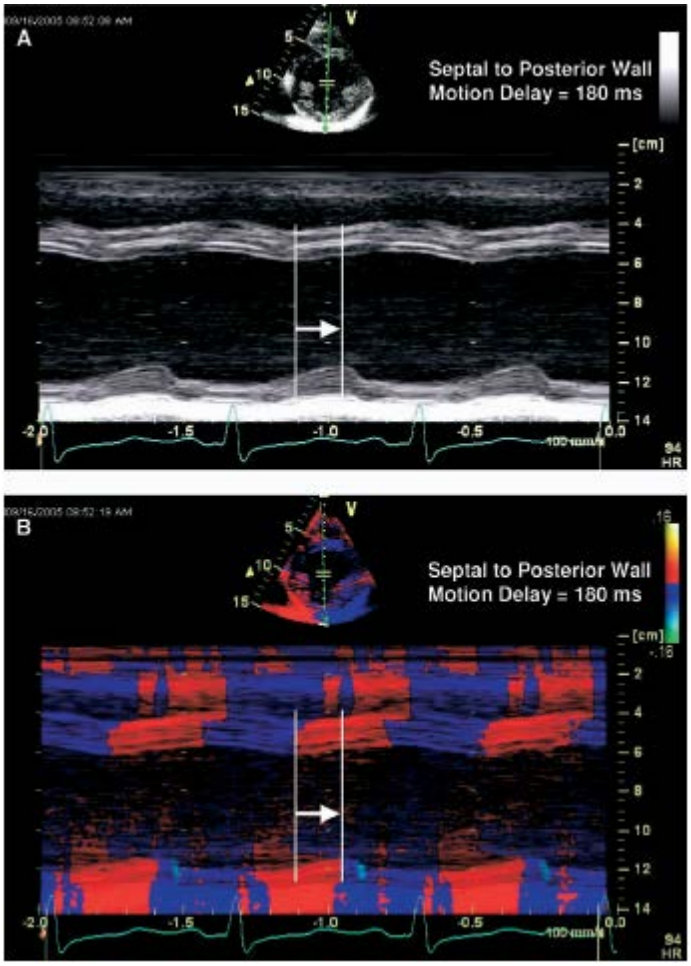

图 1 左室中段常规 M 型超声（A）和彩色组织多普勒 M 型超声显示室间隔-后壁延迟（B）为 180 毫秒，为明显的不同步（≥130 毫秒）。

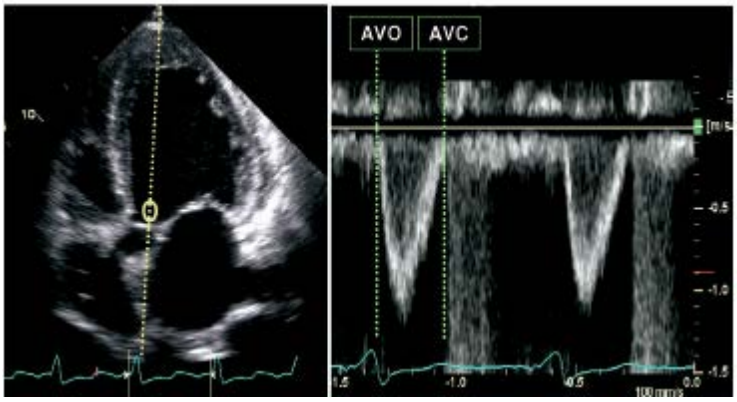

图 2 脉冲多普勒在左室流出道测量射血时间。AVC 为主动脉瓣关闭(aortic valve closure)；AVO 为主动脉瓣开放(aortic valve opening)。

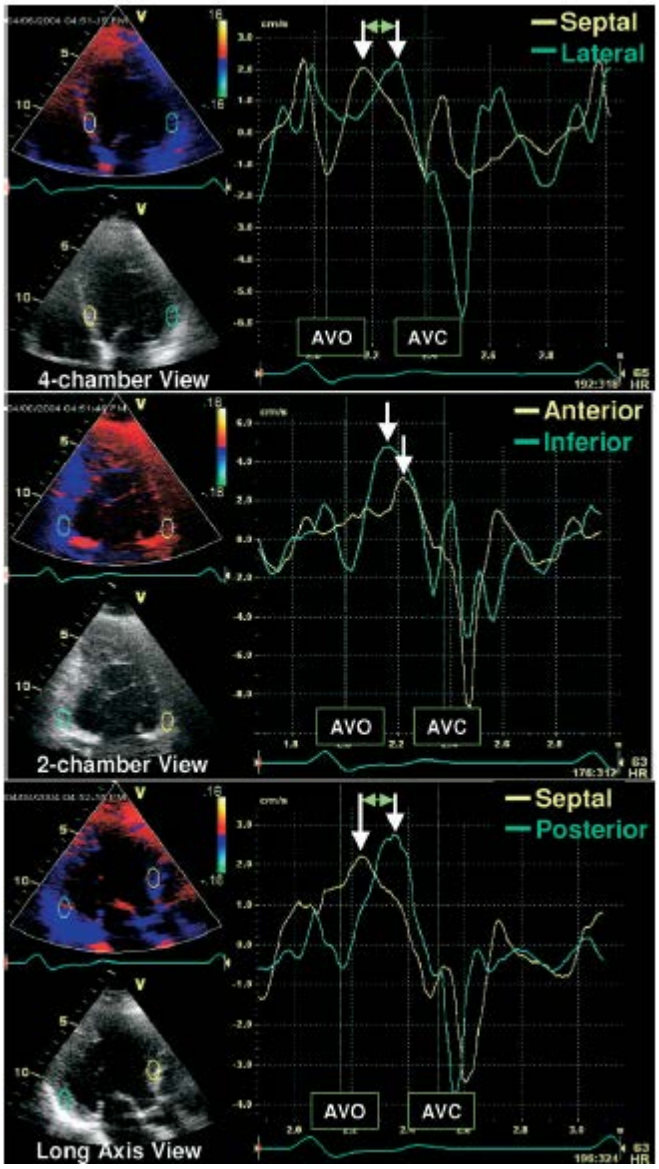

图 3 再同步化治疗有效病人的三个标准心尖切面彩色组织多普勒图。图示有代表性的基底段或中间段的时间-速度曲线。心尖长轴切面示室间隔与后壁最大延迟时间为 140ms，为明显的不同步（≥65 毫秒）。

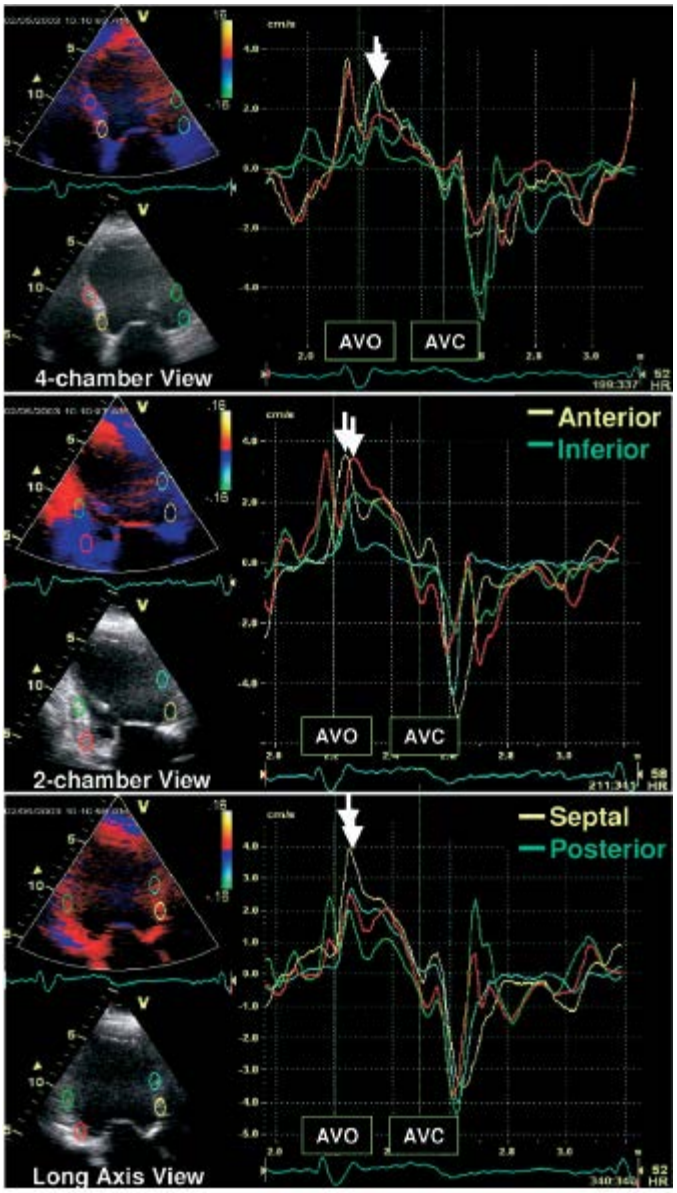

图 4 再同步化治疗无效病人的三个标准心尖切面彩色组织多普勒图。基底段和中间段的时间-速度曲线均显示相对两侧室壁的延迟不明显，小于 65 毫秒。

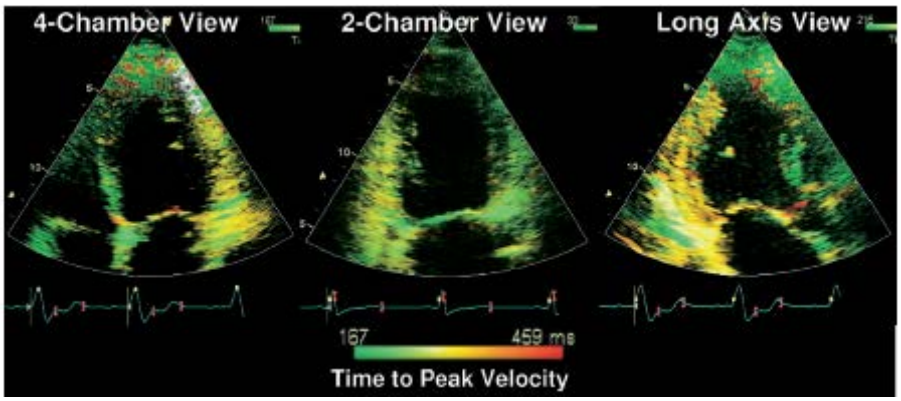

图 5 再同步化有效的收缩不同步患者三个标准心尖切面的组织多普勒图像，速度达峰之间

经彩色编码。侧壁（四腔心显示）和后壁（心尖长轴显示）为橘黄色，表明有达峰时间的延迟。

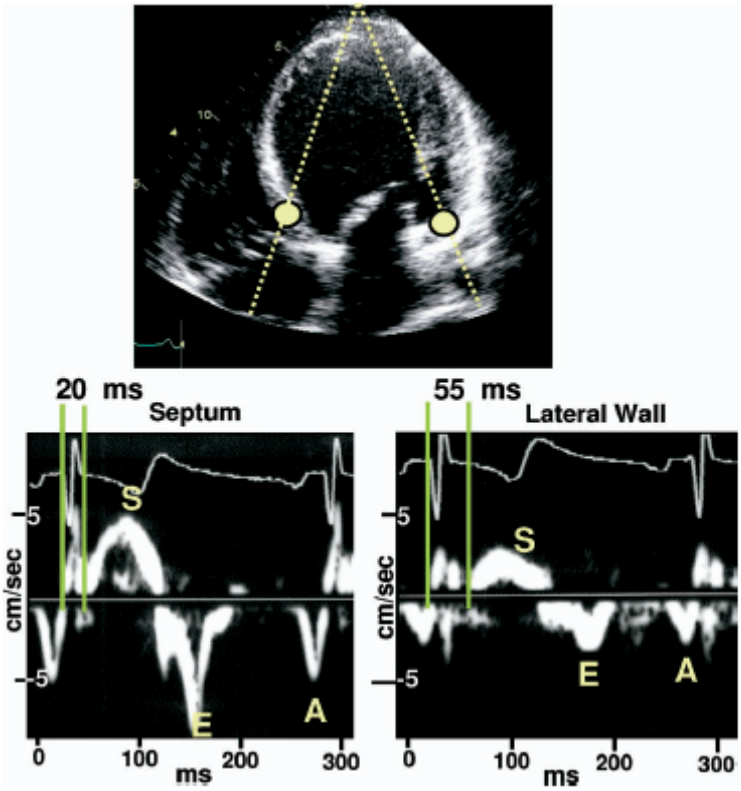

图 6 脉冲组织多普勒显示合并左束支传导阻滞的病人在同步化治疗前，侧壁与室间隔相比，收缩起始时间延迟。

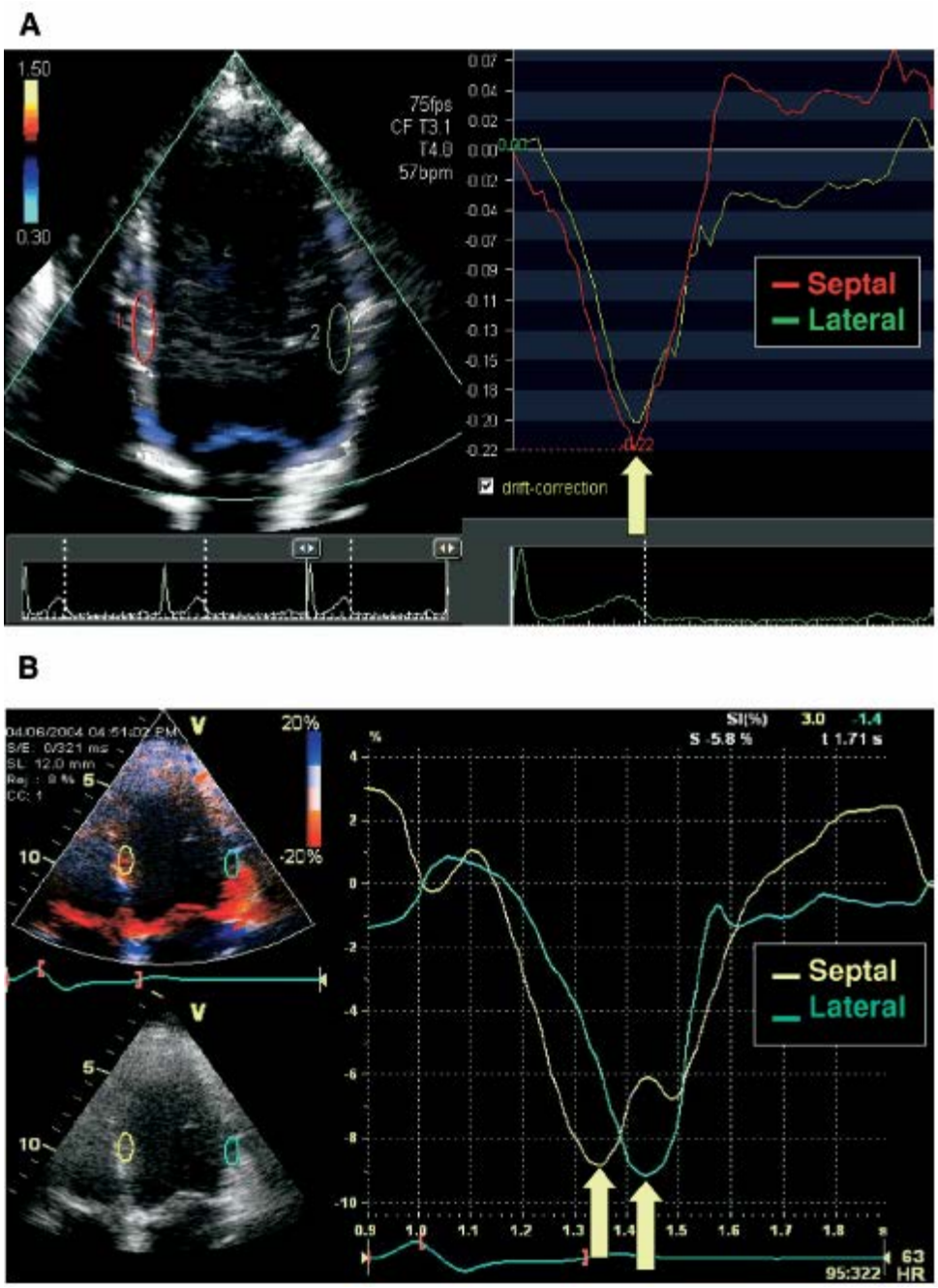

图7 组织多普勒法显像测定长轴应变，A：健康者左心室收缩； B： 再同步化治疗前左束支传导阻滞的病人。

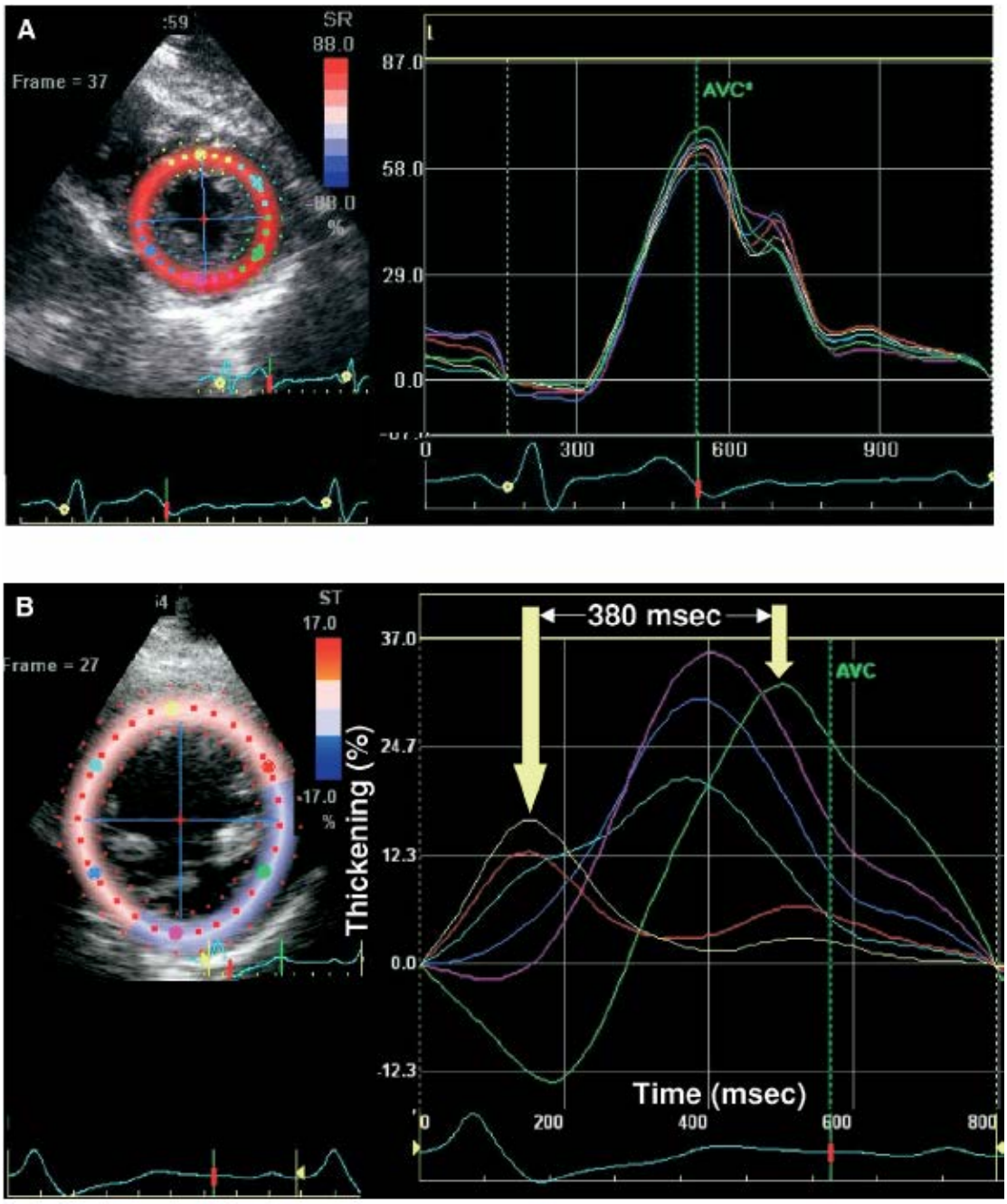

图8 斑点追踪法显示径向应变同步情况。A：健康人； B：心衰并左束支传导阻滞拟行CRT治疗前的病人存在严重的不同步。

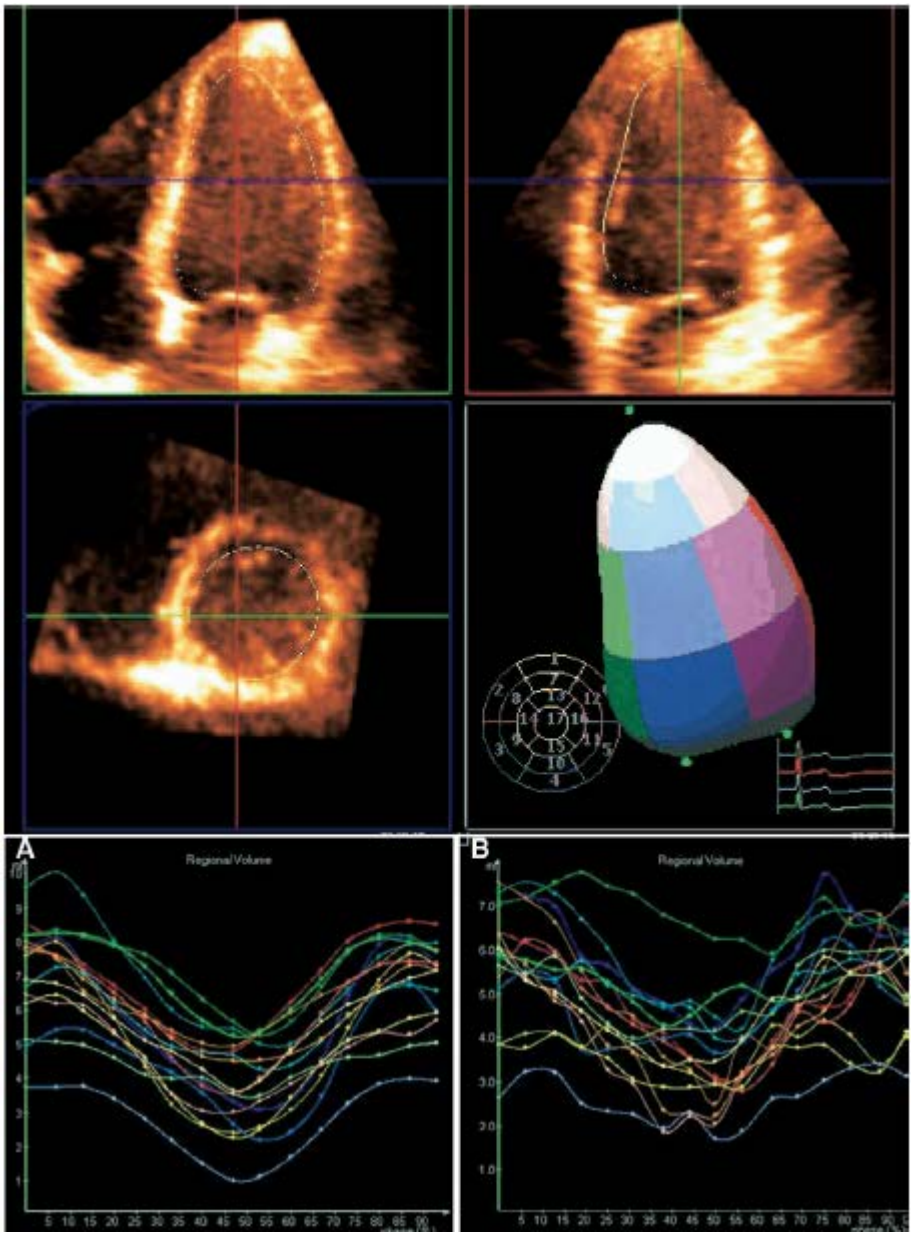

图9 三维超声心动图评价节段性容积变化。 A：健康人； B：严重不同步的病人。

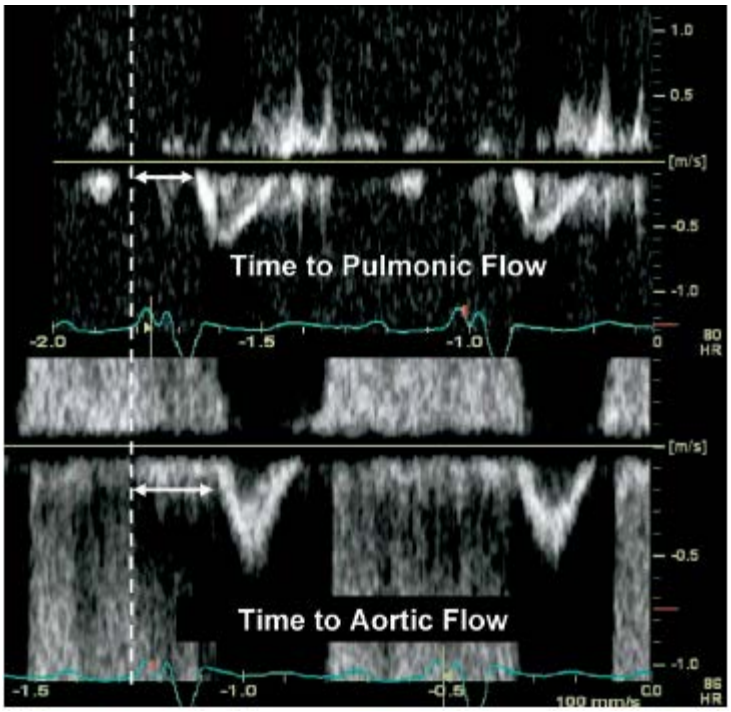

图10 右室流出道及左室流出道频谱多普勒显示左室射血明显延迟（大于40毫秒）

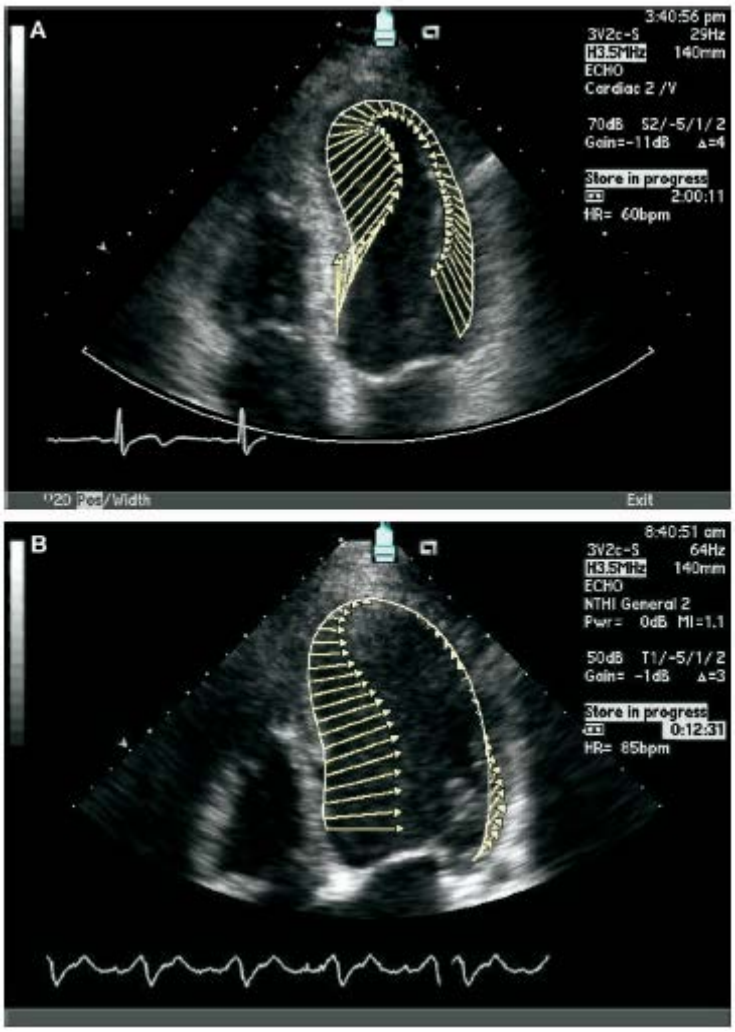

图11 速度向量成像。 A： 健康人左心室收缩同步、协调；B： 心衰并左束支传导阻滞拟CRT治疗的病人，室间隔-侧壁存在严重不同步。

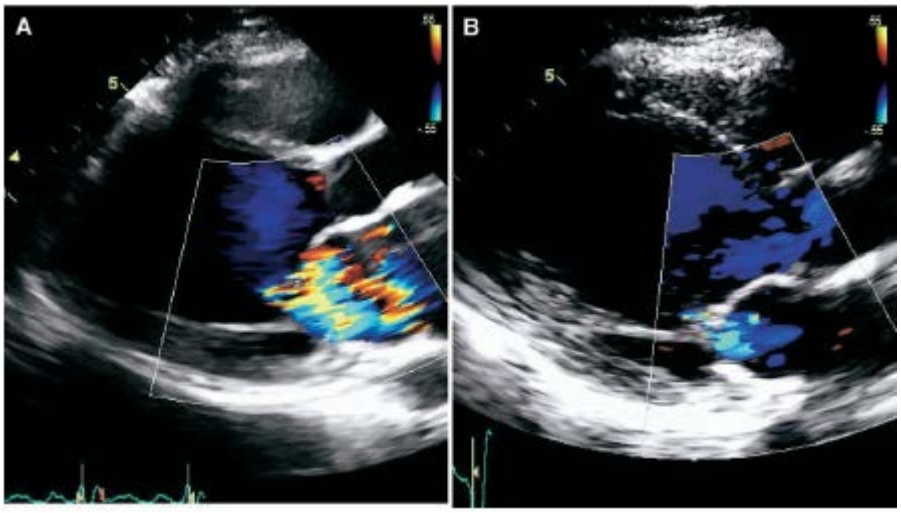

图12 胸骨旁长轴显示二尖瓣反流CRT后明显减轻。A：术前；B：术后第一天。

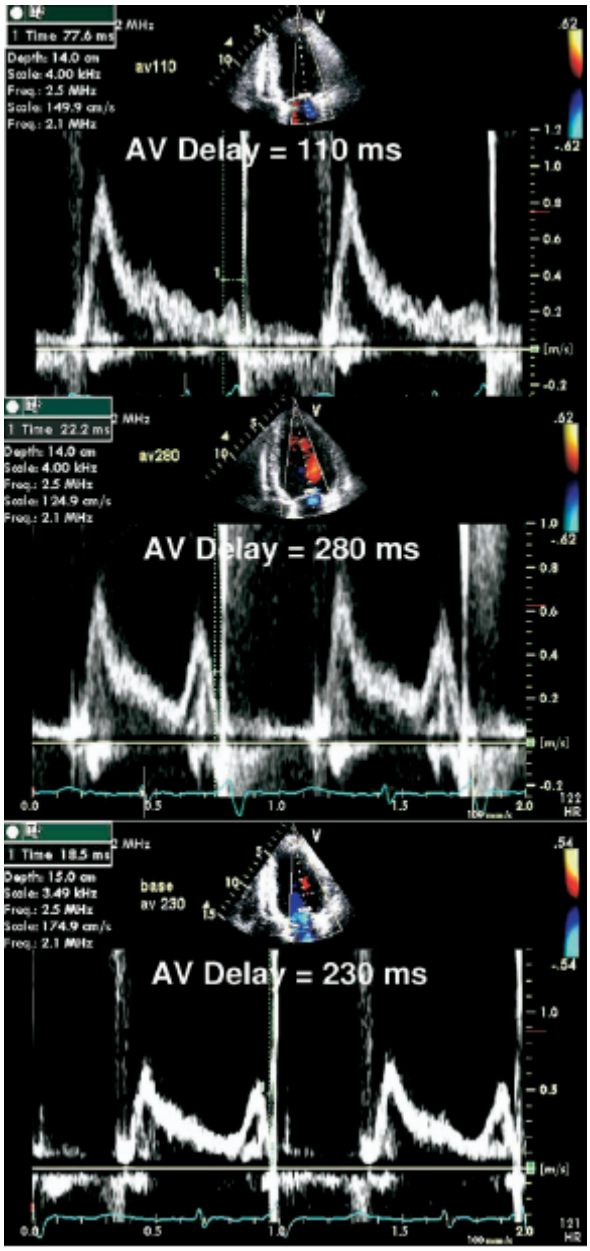

图13 二尖瓣流入道血流频谱用于AV间期优化。上：AV间期110毫秒时二尖瓣频谱A峰消失；中： AV间期280毫秒；下：AV间期230毫秒。中图和下图中心室舒张期内完成了心房收缩，左心室充盈得到改善。AV间期为230毫秒时二尖瓣开放与A波终止同时发生。

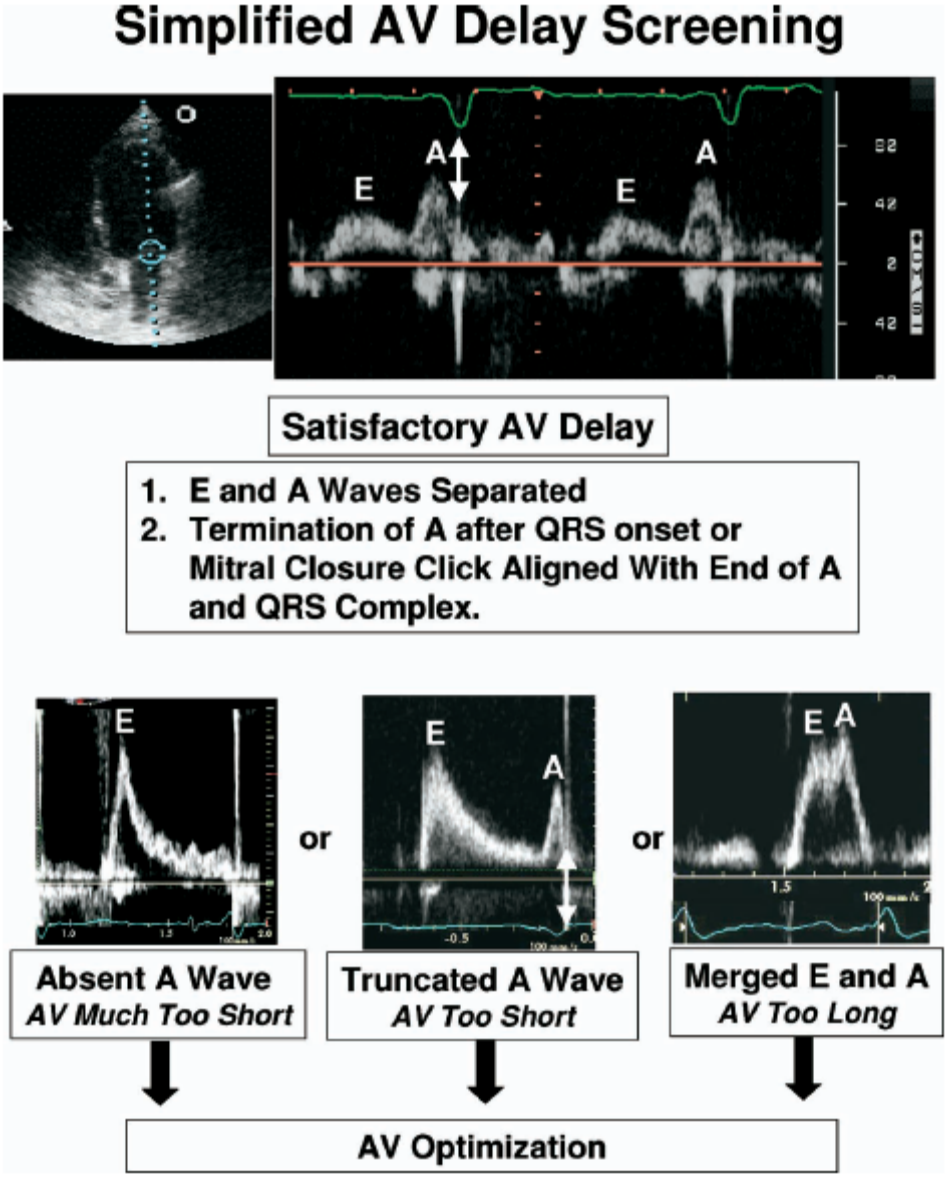

图14　利用二尖瓣流血流频谱进行简化的AV间期优化。取样容积放在二尖瓣水平，可以观察到二尖瓣关闭情况。如果E峰和A峰没有融合，且A峰在QRS波之前结束，或者二尖瓣关闭与A峰和QRS波的终止同步（通常显示为舒张功能减退I期松弛异常，E峰小于A峰）（上图），可能不需要进行优化。如果A峰提前结束、E峰和A峰融合，或者没有A峰（下图），则需要进行AV间期的优化。二尖瓣血流频谱呈舒张功能异常II期（假性正常化）或III期（限制性充盈），也需要考虑优化AV间期。

Echocardiography for Cardiac Resynchronization Therapy: Recommendations for Performance and Reporting–A Report from the American Society of Echocardiography Dyssynchrony Writing Group *Endorsed by the Heart Rhythm Society*

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Echocardiography plays an evolving and important role in the care of heart failure patients treated with biventricular pacing, or cardiac resynchronization therapy (CRT). Numerous recent published reports have utilized echocardiographic techniques to potentially aide in patient selection for CRT prior to implantation and to optimized device settings afterwards. However, no ideal approach has yet been found. This consensus report evaluates the contemporary applications of echocardiography for CRT including relative strengths and technical limitations of several techniques and proposes guidelines regarding current and possible future clinical applications. Principal methods advised to qualify abnormalities in regional ventricular activation, known as dyssynchrony, include longitudinal velocities by color-coded tissue Doppler and the difference in left ventricular to right ventricular ejection using routine pulsed Doppler, or interventricular mechanical delay. Supplemental measures of radial dynamics which may be of additive value include septal-to-posterior wall delay using M-mode in patients with non-ischemic disease with technically high quality data, or using speckle tracking radial strain. A simplified post-CRT screening for atrioventricular optimization using Doppler mitral inflow velocities is also proposed. Since this is rapidly changing field with new information being added frequently, future modification and refinements in approach are anticipated to continue.

Keywords: Echocardiography, Doppler ultrasound, Congestive Heart Failure, Pacing Therapy

Echocardiography plays an important role in the care of patients with heart failure treated with cardiac resynchronization therapy (CRT). A large number of clinical reports have utilized echocardiography before CRT implantation to assess abnormalities of mechanical activation, known as dyssynchrony, to potentially improve patient selection or guide lead placement. In addition, echocardiography has been advocated to optimize the CRT device settings afterward. The purpose of this consensus report is to evaluate the contemporary state-of-the-art applications of echocardiography for CRT and to propose guidelines regarding current and potential future clinical applications. We acknowledge that this is a relatively young and rapidly changing field with new information being discovered continually. Because no optimal approach has yet been clearly defined, the strengths and limitations of the principal current techniques will be discussed along with practical recommendations.

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CLINICAL BENEFITS OF RESYNCHRONIZATION THERAPY

CRT has had a major favorable impact on the care of patients with heart failure, left ventricular (LV) systolic dysfunction, and mechanical dyssynchrony, routinely identified by electrocardiography (ECG) as abnormal electrical activation. CRT, also referred to as biventricular pacing, has been shown in several randomized clinical trials to improve heart failure functional class, exercise capacity, and quality of life, in addition to reducing hospitalizations and prolonging survival[1-7]

Table 1 Summary of important clinical trials of cardiac resynchronization therapy

	MUSTIC	PATH-CHF	MIRACLE	MIRACLE-ICD
Inclusion criteria	NYHA III LVEF < 35% EDD > 60 mm 6-min walk < 450 m QRS ≥ 150 ms	NYHA III, IV QRS ≥ 120 ms	NYHA III, IV LVEF ≤ 35% EDD ≥ 55 mm QRS ≥ 130 ms	NYHA III, IV LVEF ≤ 35% EDD ≥ 55 mm QRS ≥ 130 ms ICD indication
Sample	58	40	453	369
End points	QOL, 6-min walk, peak VO_2, HF hospitalization	Acute hemodynamics QOL, 6-min walk, HF hospitalization	QOL, NYHA class, 6-min walk, composite	QOL, NYHA class, 6-min walk
Study design	Single-blind, randomized, crossover	Single-blind, randomized, crossover	Double-blind, randomized, parallel-controlled	Double-blind, randomized, parallel-controlled
Treatment arms	CRT vs no pacing	CRT vs no pacing	CRT vs no pacing	CRT-D vs ICD
Major findings	CRT improved all end points, reduced hospitalization	CRT improved acute hemodynamics and chronic end points	CRT improved all end points; reduced HF hospitalization	CRT improved QOL and NYHA class only, and did not impair ICD function

	CONTAK	COMPANION	CARE-HF
Inclusion criteria	NYHA II-IV LVEF ≤ 35% QRS ≥ 120 ms ICD indication	NYHA III, IV LVEF ≤ 35% QRS ≥ 120 ms	NYHA III, IV LVEF ≤ 35% QRS > 150 ms or QRS = 120-150 with dyssynchrony
Sample	333	1520	819
End points	Composite of mortality, HF hospitalization and VT/VF	Primary: all-cause mortality or hospitalization; secondary: all-cause mortality	All-cause mortality or unplanned hospitalization
Study design	Double-blind, randomized, parallel-controlled	Randomized, parallel-controlled	Randomized, parallel-controlled
Treatment arms	CRT-D vs ICD	CRT vs CRT-D vs no pacing	CRT vs no pacing
Major findings	CRT improved secondary end points; primary end points did not improve	CRT and CRT-D improved primary end point; CRT-D; reduced mortality	CRT improved primary end point and reduced all cause mortality

CRT, Cardiac resynchronization therapy; *CRT-D*, cardiac resynchronization therapy-defibrillator; *EDD*, left ventricular end-diastolic diameter; *HF*, heart failure, *ICD*, implantable cardioverter defibrillator; *LVEF*, left ventricular ejection fraction; *NYHA*, New York Heart Association; *QOL*, quality of life score, *VF*, ventricular fibrillation; *VO_2*, maximal oxygen consumption; *VT*, ventricular tachycardia.

(Table 1). Furthermore, CRT is associated with reductions in mitral regurgitation (MR) and improvements in LV function.[2,8-12] Currently approved recommendations for CRT include patients with severe heart failure: New York Heart Association (NYHA) functional class III or IV, widened QRS greater than or equal to 120 milliseconds, and LV ejection fraction (EF) less than or equal to 35%.[13] Despite the great success of randomized clinical trails, approximately 25% to 35% of patients undergoing CRT do not respond favorably. Echocardiographic and Doppler imaging techniques have emerged to play a potential role in the care of the patient with CRT. Although there are several potential reasons for nonresponse to CRT, it has been suggested that the ECG widened QRS is a suboptimal marker for dyssynchrony, and that echocardiographic quantification of dyssynchrony may potentially play a role in improving patient selection for CRT.[12,14-16] The PROSPECT study (predictors of responders to CRT) was a recent observational multicenter study from Europe, the United States, and Hong Kong.[17,18] Although final data from this study are not yet available, the preliminary findings highlighted the complexity of technical factors that influence dyssynchrony analyses and the importance of training and expertise of individual laboratories to achieve reliable results. The PROSPECT study suggested that there are technical issues related to variability that are not yet resolved, and that future work is needed to improve reproducibility of dyssynchrony analysis.

OVERVIEW OF MECHANICAL DYSSYNCHRONY

Electrical activation in the normal heart typically occurs quickly within 40 milliseconds via conduction through the Purkinje network and is associated with synchronous regional mechanical contraction. A variety of myocardial diseases induce alterations in cardiac structure and function that result in regions of early and late contraction, known as dyssynchrony.[19] Although other authors have used the term "asynchrony" interchangeably, we will use the term "dyssyn-

chrony" in this report to describe this phenomenon. Mechanical dyssynchrony is usually associated with a prolonged QRS duration on the surface ECG, although it may also exist in a subset of patients with heart failure and depressed LV function and narrow QRS by ECG.[20,21] This report will focus on patients with wide QRS duration, because this is the current clinical practice for CRT.

Three types of cardiac dyssynchrony may occur: intraventricular, interventricular, and atrioventricular (AV). Abnormalities of timing of regional mechanical LV activation, known as intraventricular dyssynchrony, appear to be the principal factor associated with contractile impairment and affected by CRT. Accordingly, many echocardiographic Doppler parameters focus on intraventricular dyssynchrony, and we will use the term "dyssynchrony" throughout this report when referring to "intraventricular dyssynchrony," unless otherwise stated. The classic type of dyssynchrony resulting from abnormal electrical activation is seen with left bundle branch block. The typical pattern seen with left bundle branch block is early activation of the interventricular septum and late activation of the posterior and lateral LV walls.[19] The early septal contraction occurs before normal ejection when LV pressure is low and does not contribute to ejection. This process generates heterogeneous stress and strain in the LV, with one wall exerting forces on the contralateral wall. Typically early septal contraction causes posterior-lateral stretching or thinning, followed by late posterior-lateral contraction causing septal stretching or thinning.[22] Dyssynchrony results in inefficient LV systolic performance, increases in end-systolic volume and wall stress, and delayed relaxation that is thought to affect biological signaling processes involved in regulating perfusion and gene expression.[23] Improvements in LV synchrony are associated with LV functional improvements and reduction in MR.[8,24-28]

GENERAL APPROACH TO QUANTIFYING MECHANICAL DYSSYNCHRONY

Because the vast majority of patients with wide QRS appear to have mechanical dyssynchrony, an important goal of imaging is to improve patient selection for CRT by identifying the subset of patients with wide QRS but no mechanical dyssynchrony. The pathophysiologic reason for this scenario is unclear, but it appears that patients with minimal to no dyssynchrony have a lower probability of response to CRT and appear to have a poor prognosis after CRT.[15] There are other reasons for not responding to CRT, including ischemic disease with too much scar to reverse remodel, subsequent infarction after CRT, suboptimal lead placement, and other factors not yet defined.[24,29-33] Accordingly, the absence of dyssynchrony is only one factor for nonresponse, but one that potentially can be identified prospectively by echocardiographic Doppler methods.

Results from the PROSPECT study illustrated that technical factors of individual echocardiographic Doppler methods, such as feasibility and reproducibility, affect results in a multicenter setting.[17,18] Quantifying mechanical dyssynchrony in a series of patients with heart failure is complex, and no single ideal method currently exists. However, a practical approach that considers several factors is currently recommended to assist in determining that a patient has or does not have significant dyssynchrony. Ambiguities that may occur in analysis using different approaches must be adjudicated on a case-by-case basis. A reasonable starting point is to examine the routine 2-dimensional (2D) echocardiographic images. Trained observers can often assess dyssynchrony visually as an early septal in-and-out motion described as septal flash or bounce in typical left bundle branch block dyssynchrony. Because the presence or absence of dyssynchrony may be subtle in many patients with severe heart failure, visual assessment should not stand alone and the use of quantitative echocardiographic Doppler tools is advocated.

M-MODE

The technically simplest approach to quantify LV dyssynchrony is with conventional M-mode echocardiography that records septal-to-posterior wall-motion delay (Figure 1, *A*).

Step 1: Select either the parasternal long-axis or short-axis views.

Step 2: Position the M-mode cursor at the midventricular level (papillary muscle level).

Step 3: Set sweep speed to 50 to 100 mm/s.

Step 4: Identify the time delay from peak inward septal motion to peak inward posterior wall.

Pitzalis et al reported a cut-off value of greater than or equal to 130 milliseconds as a marker of LV dyssynchrony in a pilot series of 20 patients principally with nonischemic cardiomyopathy with a sensitivity of 100% and specificity of 63% to predict a greater than or equal to 15% decrease in LV end- systolic volume index, and improvements in clinical outcome.[34,35] Longer delays in septal to posterior wall-motion delay were associated with greater reverse remodeling. Measurement of the septal-to-posterior wall-motion delay by M-mode may be difficult in many patients because of complex septal motion that is both active and passive–wall-motion abnormalities involving the septum or posterior wall. Marcus et al highlighted these limitations in an analysis of M-mode data from 79 patients in the CONTAK-CD trial.[36] They found the reproducibility of M-mode measurements to be unsatisfactory, with responders (defined as ≥15% reduction in LV end-systolic volume) having septal-to-posterior wall-motion delays similar to nonresponders. The PROSPECT study also identified a high degree of variability in analysis.[17,18] Therefore, M-mode is not advocated to be used in isolation to quantify dyssynchrony, but may be considered as supplemental to other approaches, such as tissue Doppler (TD). In particular, the utility of M-mode in patients with ischemic cardiomyopathy has not been well demonstrated.

COLOR TD M-MODE

The addition of color TD M-mode is a useful adjunct to M-mode determination of LV dyssynchrony (Figure 1, *B*). Changes in direction are color coded, which may aid in identifying the transition from inward to outward motion in the septum and posterior wall. The same septal-to-posterior wall-motion delay greater than or equal to 130 milliseconds is considered to be significant dyssynchrony, although this method is affected by similar limitations with routine M-mode as described above.

LONGITUDINAL TD VELOCITY

The largest body of literature to quantify dyssynchrony is represented by the assessment of longitudinal LV shortening velocities using TD from the apical windows.[14-16,37-49] This is the principal method currently in clinical use, although it has limitations discussed subsequently. There are two basic approaches: color-coded or pulsed TD.

COLOR TD DATA ACQUISITION

Color TD data acquisition is simpler and more practical than pulsed TD and is the preferred method by consensus of this committee if

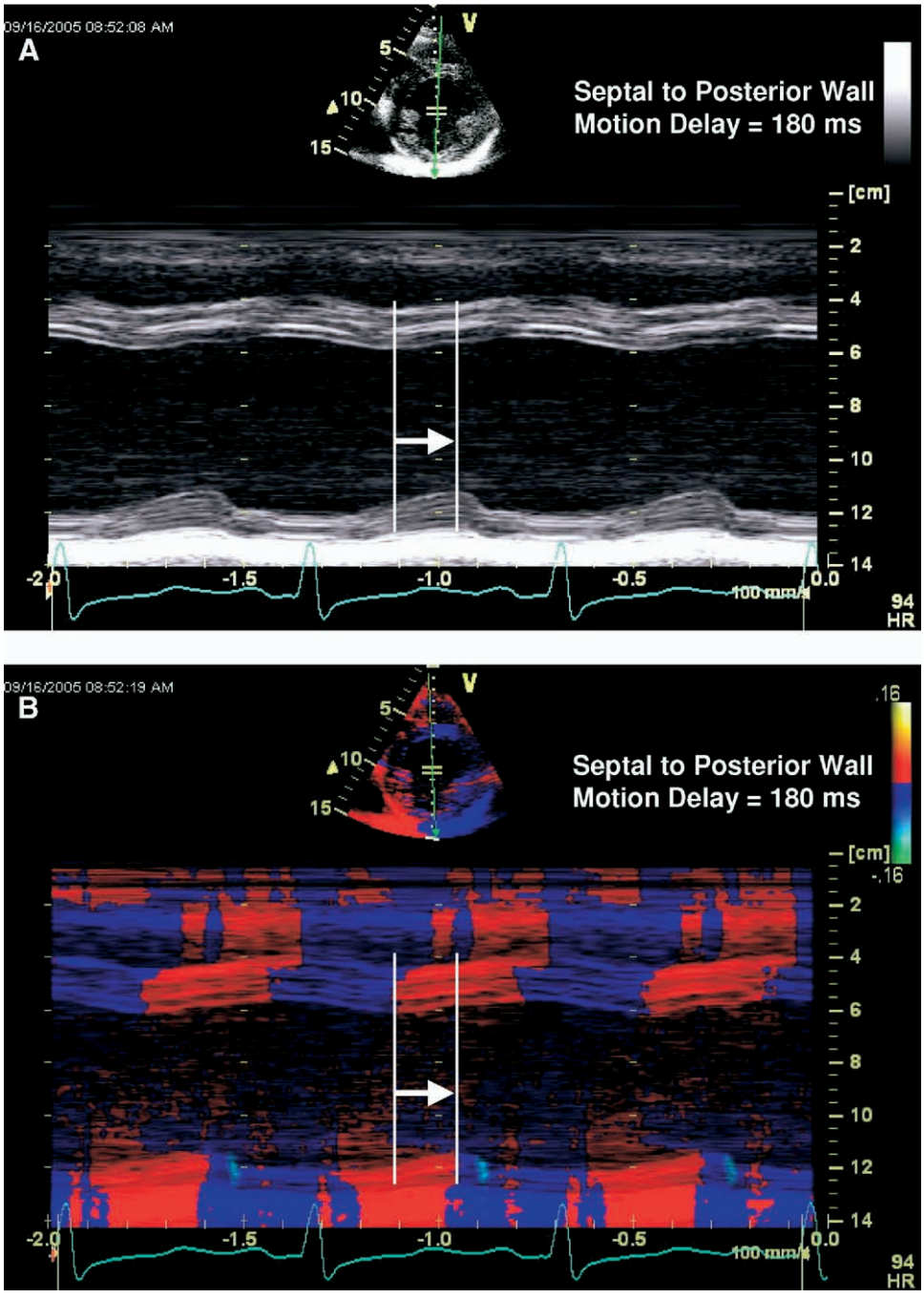

Figure 1 Routine M-mode (**A**) at midventricular level and color-coded tissue Doppler M-mode (**B**) demonstrating septal to posterior wall delay of 180 milliseconds, consistent with significant dyssynchrony (≥130 milliseconds).

high frame rate color TD echocardiographic equipment is available. High frame–rate color TD, usually greater than 90 frames/s, is available in several major equipment vendors with recent hardware and software. Individual variations in color TD between ultrasound systems may exist, but these details have not yet been elucidated.

Step 1: Adjust the ECG to be noise free with a delineated QRS waveform.

Step 2: Optimize 2D imaging to insure maximal apical-to-near field left atrial imaging, with overall gain and time gain control settings adjusted for clear myocardial definition.

Step 3: Position the LV cavity in the center of the sector and aligned as vertically as possible, to allow for the optimal Doppler angle of incidence with LV longitudinal motion.

Step 4: Set the depth to include the level of the mitral annulus.

Step 5: Activate color TD and adjust the sector to include the entire LV with a goal of achieving high frame rates (usually >90 frames/s). Decrease depth and sector width to focus on the LV to increase frame rates, as needed. Adjust overall color gain for clear delineation of the myocardium. If available, the online color coding of time to peak velocity data may be activated.

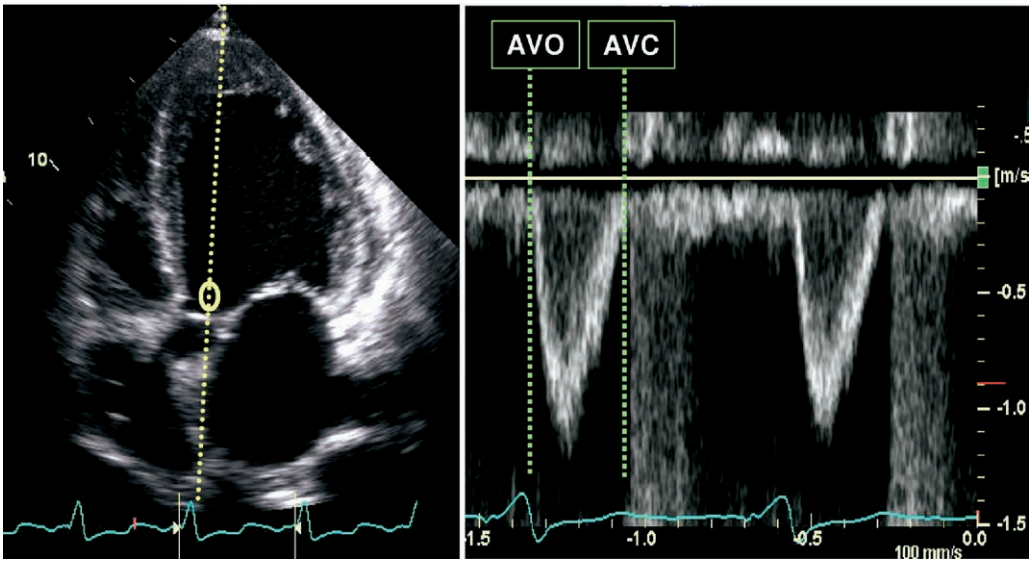

Figure 2 Determination of left ventricular ejection interval from pulsed Doppler of outflow tract. *AVC*, Aortic valve closure; *AVO*, aortic valve opening.

Step 6: Suspend patient breathing. Because low velocity TD data are affected by respiratory motion, we recommend that patients be instructed to hold their breath transiently if they are able, while a 3- to 5-beat digital capture is performed. This is usually at end expiration, but may be the phase with the optimal image quality. The number of beats captured should be increased if atrial or ventricular premature complexes are present.

Step 7: Record 3 standard imaging planes: apical 4-chamber view, apical 2-chamber view, and apical long-axis view.

Step 8: Determine the LV ejection interval. This is usually done using pulsed Doppler from an apical 5-chamber or apical long-axis view where the LV outflow tract is seen and velocity recorded (Figure 2).

COLOR TD DATA ANALYSIS

A major advantage of color DTI is the ability to analyze time-velocity data offline. The details for analysis vary by ultrasound vendor, but the general steps are similar.

Step 1: Determine the timing of LV ejection, usually from the beginning to the end of pulsed Doppler flow of the LV outflow tract. The details vary according to ultrasound system used, but timing usually is performed using the ECG as a time marker. The timing of beginning ejection to end ejection is then superimposed as the ejection interval on the subsequent time-velocity curve analysis.

Step 2: Size and place regions of interest (a minimum of 5 × 10 mm to 7 × 15 mm) in the basal and midregion of opposing LV walls (4 regions/view) to determine time-velocity plots.

Step 3: If possible, identify components of velocity curve, as a check for physiologic signal quality. These include isovolumic contraction velocity (usually <60 milliseconds from the onset of the QRS), the systolic wave, or S wave, moving toward the transducer and the early diastolic, or E wave, and late diastolic, or A wave, moving away from the transducer (Figures 3 and 4).

Step 4: Manually adjust the regions of interest within the segment both longitudinally and side-to-side within the LV wall to identify the site where the peak velocity during ejection is most reproducible. This is an important step to search for the most reproducible peak of greatest height, in particular where there is more than one peak or signal noise. If fine tuning of the region of interest fails to produce a single reproducible peak during ejection, the earlier peak is chosen if there are two or more peaks of the same height.

Step 5: Determine time from onset of the QRS complex to the peak systolic velocity for each region: 4 segments per view, for each of 3 views, for a total of 12 segments. An alternative is to determine the difference in the time to peak S wave from opposing walls, as described in the opposing wall delay method below. This is simply the time from the S wave of one wall to the S wave of the opposing wall on the same cineloops, and does not require measuring the onset from the QRS.

Step 6: Average the time to peak values in captured beats to improve reproducibility, because beat-to-beat variability may occur. A minimum of averaging 3 to 5 beats is recommended, with the number of averaged beats increased if beat-to-beat variability is encountered, excluding sequences with atrial or ventricular premature complexes. Analysis of TD data in atrial fibrillation is especially complex and problematic, and no data are currently available to support dyssynchrony analysis in this scenario.

POSTSYSTOLIC SHORTENING VELOCITIES

Some previous studies have included postsystolic shortening (positive myocardial velocity after aortic valve closure, which may be greater than the ejection peak) in their dyssynchrony analysis.[47] The greatest sensitivity and specificity for predicting response to CRT appears to be attained when limiting peak longitudinal velocities for dyssynchrony analysis to the interval from aortic valve opening to aortic valve closure.[37,43] Notabartolo et al[47] measured the maximal difference in the time to peak systolic velocity including postsystolic shortening from the 6 basal segments. An average cut-off value greater than 110 milliseconds has a high sensitivity at 97%, but decreased specificity at 55% to predict LV reverse remodeling. Although the optimal approach has not yet been completely clarified, the current weight of evidence favors analysis of peak velocities during the ejection interval.

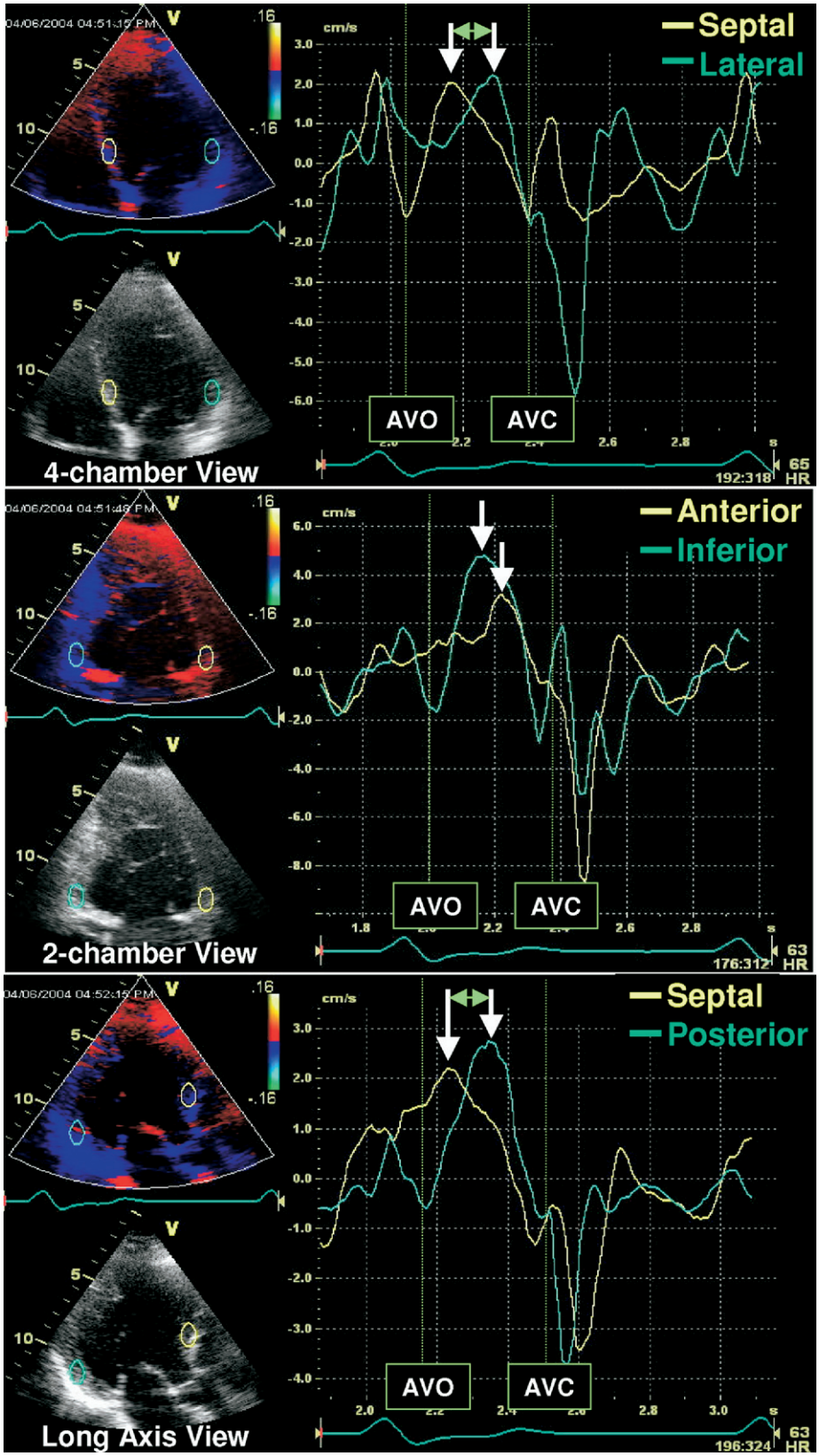

Figure 3 Color-coded tissue Doppler study from 3 standard apical views of patient who responded to resynchronization therapy. Time-velocity curves from representative basal or midlevels are shown. Maximum opposing wall delay was seen in apical long-axis view of 140 milliseconds between septum and posterior wall, consistent with significant dyssynchrony (≥65 milliseconds).

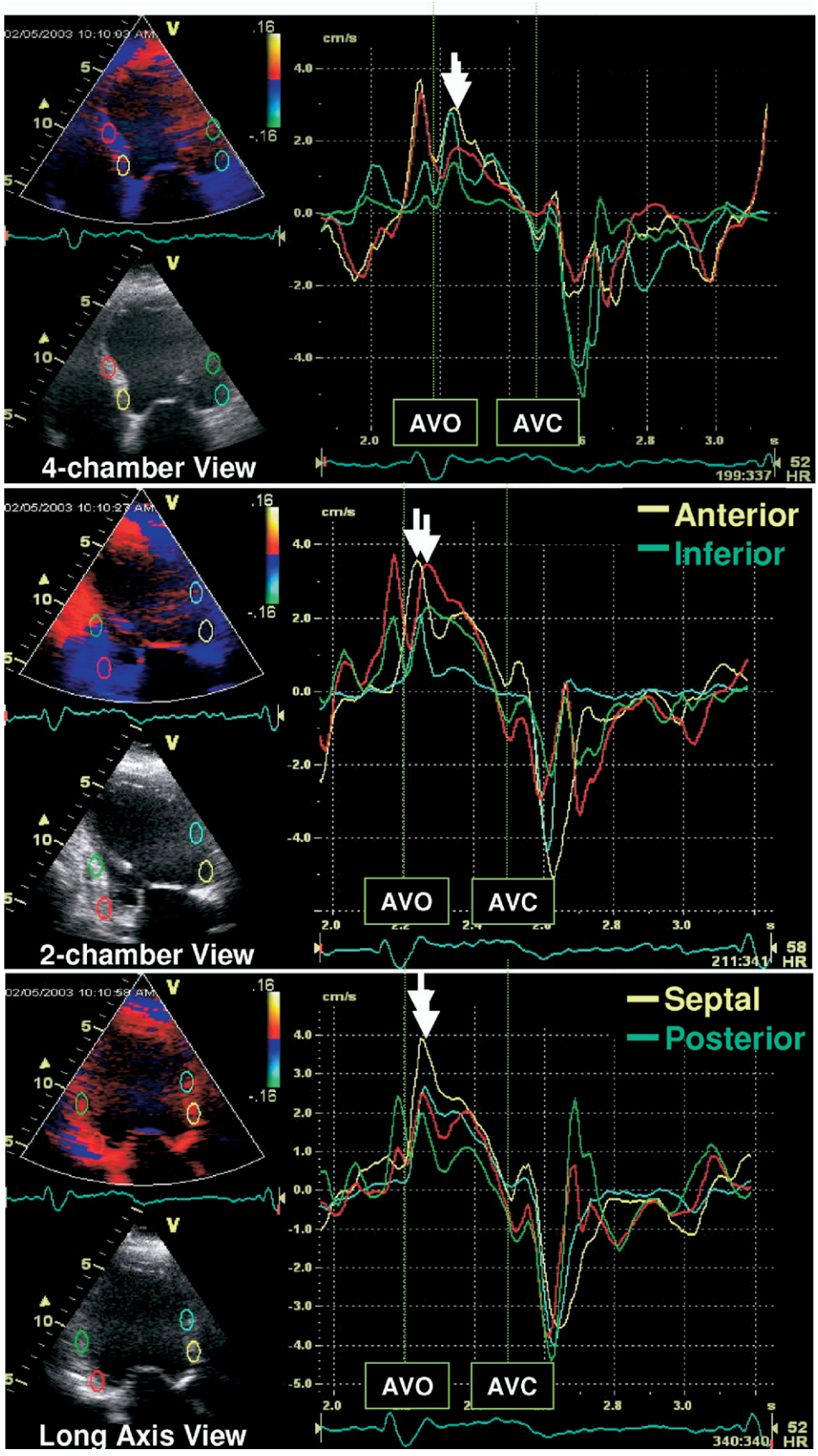

Figure 4 Color-coded tissue Doppler study from 3 standard apical views of patient who did not respond to resynchronization therapy. Time-velocity curves from both basal and midlevels show no significant opposing wall delay less than 65 milliseconds.

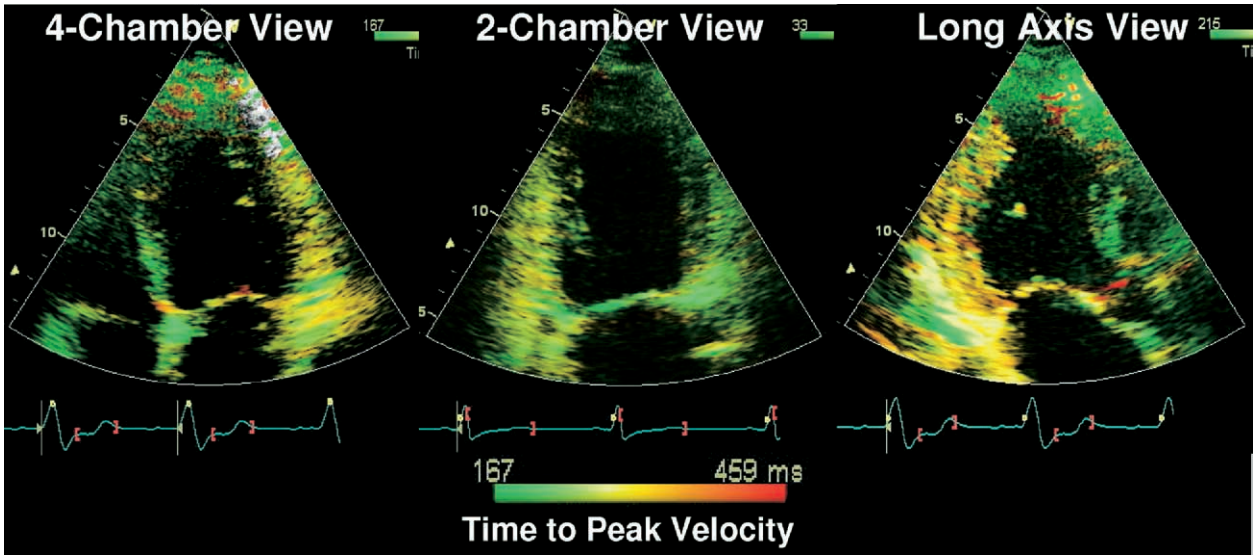

Figure 5 Tissue Doppler study from 3 standard apical views demonstrating color coding of time to peak velocity data from patient with dyssynchrony who responded to resynchronization therapy. Lateral wall (4-chamber view) and posterior wall (apical long-axis views) are color-coded *yellow-orange*, indicating delay in time to peak velocity.

CLINICAL STUDIES USING COLOR TD

The majority of studies have used color-coded TD to assess LV dyssynchrony and predict outcome, and it is the consensus of this writing group that this is currently the preferred approach. The simplest TD approach to identify LV dyssynchrony by color-coded TD uses the basal segments of the apical 4-chamber view to measure the septal-to-lateral delay, known as the two-site method.[15] Subsequently, a 4-segment model was applied that included 4 basal segments (septal, lateral, inferior, and anterior). An opposing wall delay greater than or equal to 65 milliseconds allowed prediction of both clinical response to CRT (defined by an improvement in NYHA class and 6-minute walking distance) and reverse remodeling (defined as a ≥15% reduction in LV end-systolic volume).[15] In addition, patients with LV dyssynchrony greater than or equal to 65 milliseconds had a favorable prognosis after CRT.[15,48] An extension of this opposing wall delay method has included data from the 3 standard apical views: 4-chamber, 2-chamber, and long-axis. The maximum difference in time-to-peak velocity values among the 4 sites from each of the 3 apical views is determined as the maximal opposing wall delay. An important feature of this 3-view model is that it includes the anterior-septum and posterior walls seen in the apical long-axis view, which often has dyssynchrony. Yu et al developed a 12-segment SD model using color TD that also integrates information from the same 3 apical views (4-chamber, 2-chamber, and long-axis).[31,43] The mechanical dyssynchrony index, also known as the Yu index, was derived from calculating the SD of the time-to-peak systolic velocity in the ejection phase 12-site standard deviation.[31,43,49] A 12-site standard deviation cut-off value of greater than or equal to 33 milliseconds was derived from the healthy population to signify mechanical dyssynchrony. To predict LV reverse remodeling (defined as a ≥15% reduction in LV end-systolic volume) in patients with a QRS duration greater than 150 milliseconds, this cut-off value has a sensitivity of 100% and specificity of 78%. For patients with a borderline prolongation of QRS duration of 120 to 150 milliseconds, the sensitivity is 83% and specificity is 86%.[49] An alternate method is to calculate the maximal difference in the time to peak systolic velocity among all segments, where a cut-off value of greater than or equal to 100 milliseconds predicts response to CRT.[31,43] The PROSPECT study reported that the 12-site time-to-peak SD had a lower yield and higher variability than more simple approaches, which illustrates its disadvantage as a more technically demanding approach.[18]

An extension of TD is automated color coding of time-to-peak velocity data. One method is known as tissue synchronization imaging (TSI) (Figure 5). This technology adds a color-coded overlay onto 2D images for a visual identification of regional mechanical delay. Timing should focus on the ejection period and exclude early isovolumic contraction and late postsystolic shortening. Gorcsan et al used TSI color coding to guide placement of regions of interest and assess an antero-septal-to-posterior wall delay greater than or equal to 65 milliseconds from time-velocity curves to predict acute improvement in stroke volume after CRT.[12] Yu et al also used TSI in 56 patients and found the Ts-SD derived by TSI from 12 LV segments had a highest receiver operating characteristic curve area of 0.90. Inclusion of postsystolic shortening in the model significantly reduced the receiver operating characteristic curve area to 0.69. Furthermore, all of the TSI parameters showed a slight, but consistently lower, predictive value than data derived directly from the time-velocity curves.[50] Thus, it is recommended that myocardial time-velocity curves be examined with adjustment of regions of interest as described above to ensure the accuracy of the true peak velocities when TSI is used.

PULSED TD

Pulsed TD has been described as a means to assess dyssynchrony and is available on most echocardiography systems (Figure 6). Briefly, pulsed TD presets must be optimized on the echocardiographic system as recommended by the individual manufacturers. The general approach is as described above in the step-by-step color TD data acquisition and analysis sections, with modifications. The pulsed sample volume is set to approximately 1-cm length, the velocity scale set to maximize the time-velocity curve, and the

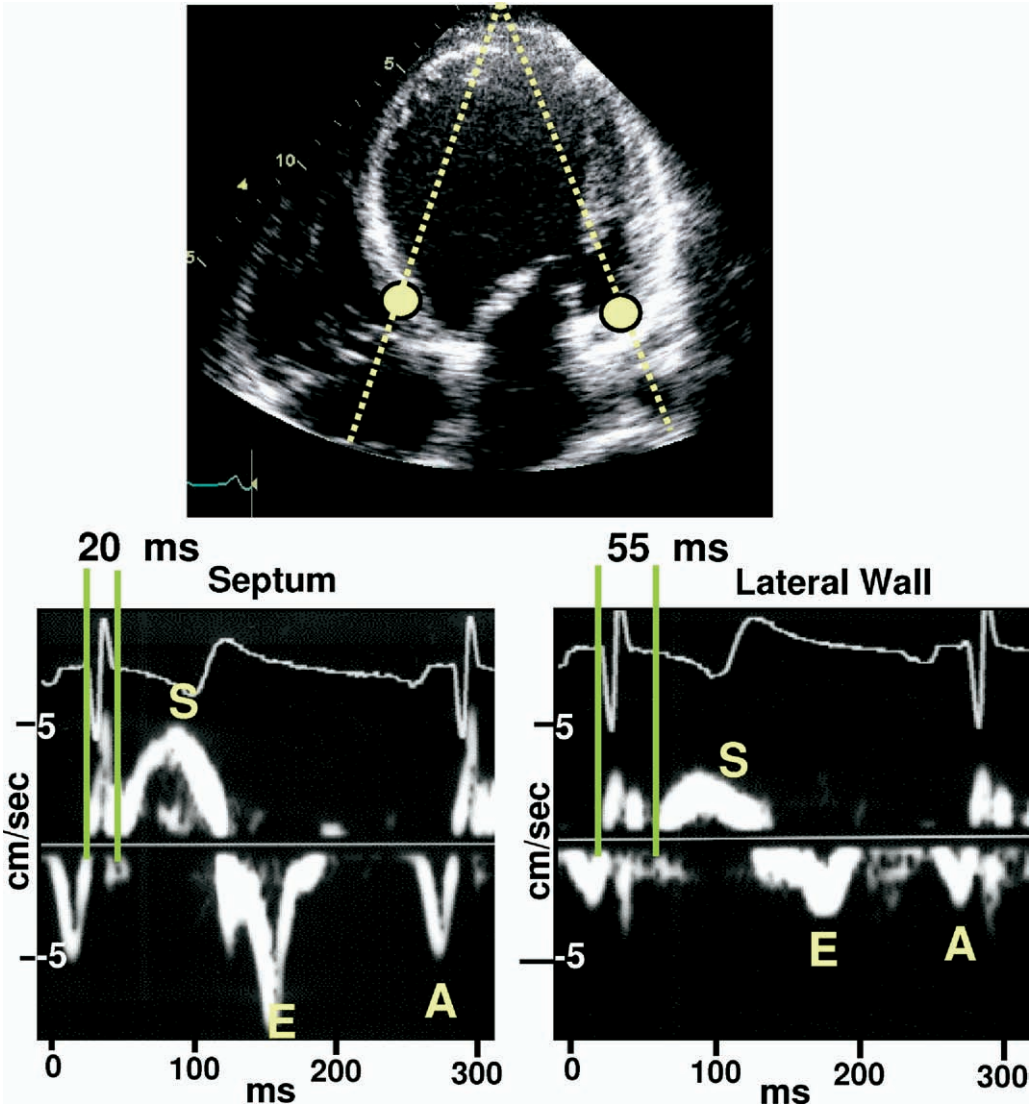

Figure 6 Pulsed tissue Doppler demonstrating dyssynchrony with delayed time to onset systolic velocity in lateral wall, as compared with septum in patient with left bundle branch block before resynchronization therapy.

sweep speed set to 50 to 100 mm/s. Unlike offline color TD data analysis, the step where the sample volume is moved within the segment to search for a reproducible time-velocity signal must be done online. This is a major disadvantage of pulsed TD because it is time-consuming and susceptible to influences of breathing, patient movement, and alterations in heart rate. In addition, the timing of the ejection interval must be transferred manually. Furthermore, the peak velocity may be difficult to identify because of a broad spectral display with a plateau during systole. Because of these technical limitations, color-coded TD is the approach preferred by this writing group. Currently, clinical studies of pulsed TD to predict response to CRT are less numerous than those using color TD. Penicka et al used pulsed wave TD to measure the time of onset of the systolic signal of basal segments from the apical 4-chamber and long-axis views and the lateral right ventricular (RV) wall.[51] Using a composite index of interventricular and intraventricular dyssynchrony longer than 100 milliseconds, they achieved 88% accuracy in identifying all but 6 patients who responded to CRT.

TD LONGITUDINAL STRAIN, STRAIN RATE, AND DISPLACEMENT

Strain and strain rate imaging have the theoretic advantage of differentiating active myocardial contraction or deformation from passive translational movement and have been utilized to identify dyssynchrony.[40,42,52] Longitudinal strain is calculated linearly from TD velocity data as percent shortening (Figure 7). However, TD longitudinal strain can be technically challenging because strain is calculated along scan lines, is Doppler angle dependent, and is difficult in patients with spherical LV geometry, often encountered in severe heart failure. Comparing myocardial velocities and strain rate, Breithardt et al found an association between regional myocardial motion (expressed by velocity parameters) and deformation (expressed by strain rate imaging parameters).[52] They concluded that the degree of dyssynchrony was not completely represented by the timing of myocardial velocity, particularly in ischemic heart disease, and that the timing of deformation should be the preferred modality. Sogaard et al found that the extent of delayed

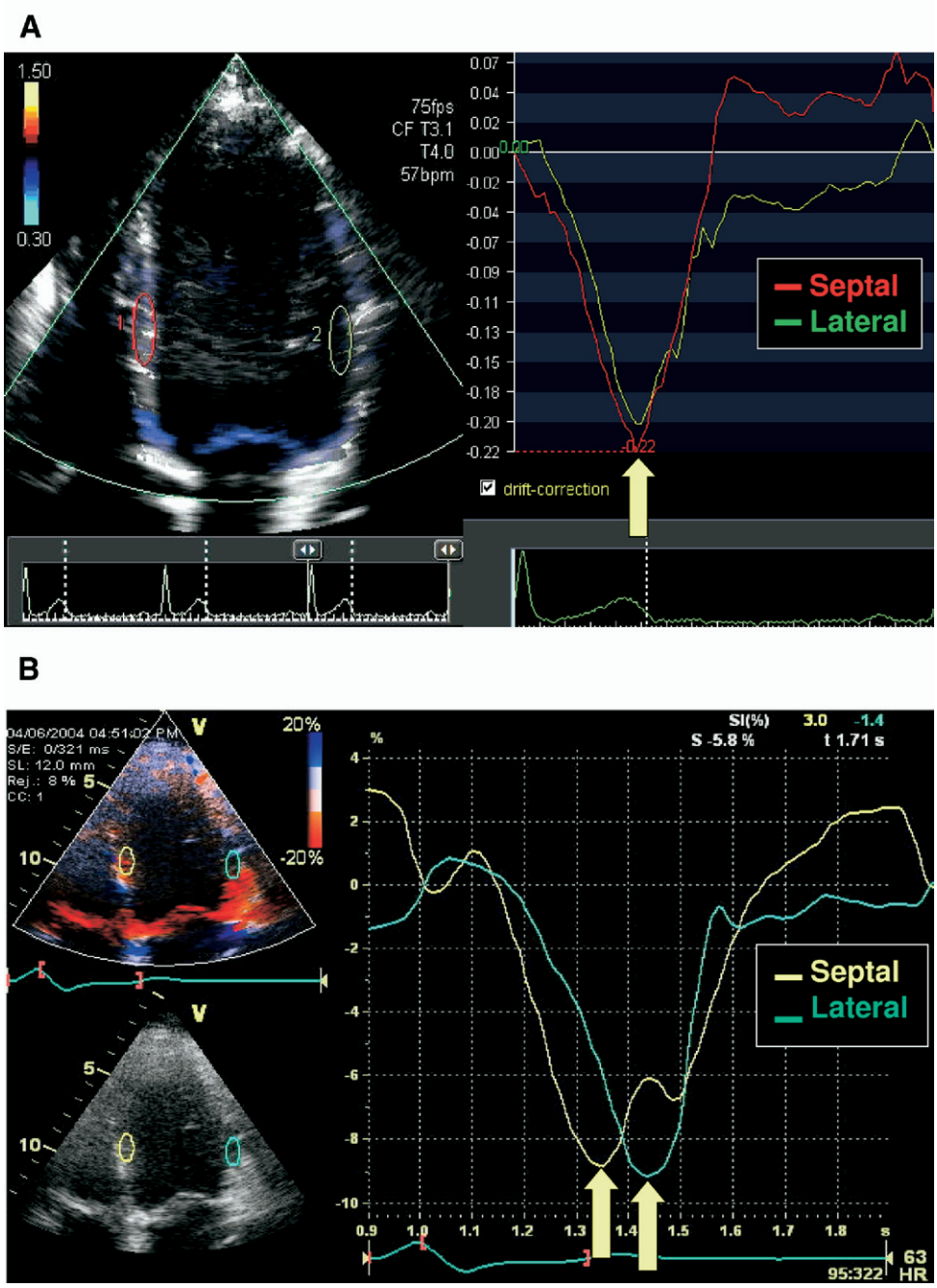

Figure 7 Doppler tissue images demonstrating longitudinal strain in healthy synchronous patient (**A**) and in patient with left bundle branch block before (**B**) resynchronization therapy.

longitudinal contraction at the base predicted improvement in EF after CRT.[41,42] However, Yu et al demonstrated that parameters of strain rate imaging are not useful to predict reverse remodeling response.[43,44,53] Currently, TD strain rate is restricted by a poor signal-to-noise ratio, which adversely affects reproducibility. On the other hand, improvements in strain analysis, including software developments such as strain determined by speckle tracking of routine gray-scale images, are promising as useful markers of systolic dyssynchrony.[54]

Displacement imaging uses TD data to calculate the distance of myocardial movement, and is typically color coded and overlaid onto 2D images. The signal-to-noise ratio is more favorable than strain or strain rate imaging, but displacement is also affected by passive motion, and the Doppler angle of incidence. Improvements in displacement or tissue tracking have been described after CRT, however, cut-off values for predicting response and clinical outcomes after CRT have not yet been established.[42]

RADIAL STRAIN

Because radial thickening is a major vector of LV contraction, and short-axis dynamics are important markers of dyssynchrony,[55] it is

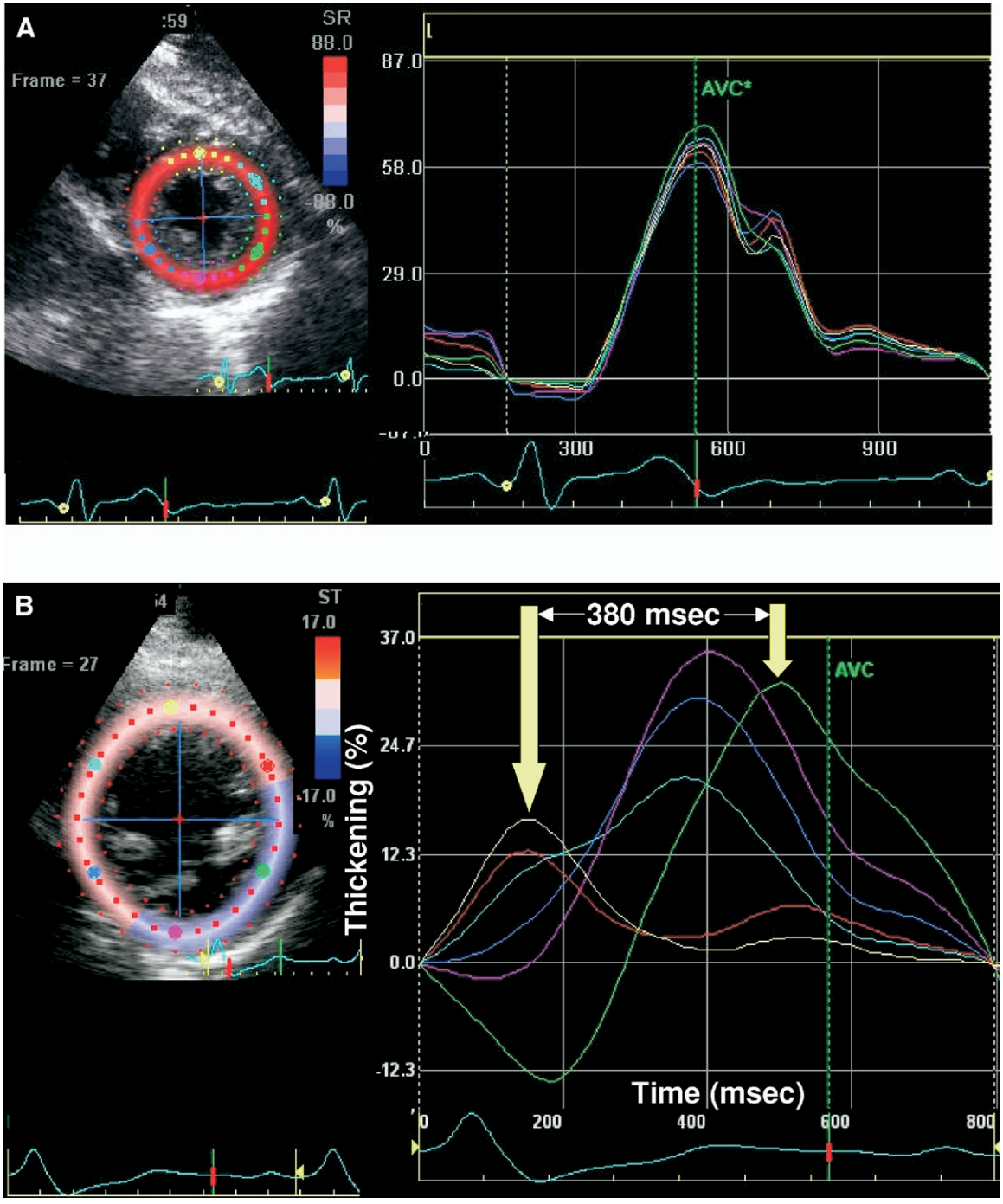

Figure 8 Speckle-tracking images demonstrating synchrony of peak segmental radial strain in healthy individual (**A**) and severe dyssynchrony in patient with heart failure and left bundle branch block (*LBBB*) referred for resynchronization therapy (**B**).

reasonable to utilize this information in a comprehensive examination. Strain has an advantage over M-mode of differentiating active from passive motion and identifying radial mechanical activation.[56] Dohi et al first used TD strain to quantify radial mechanical dyssynchrony in 38 patients who underwent CRT.[57] Radial strain was calculated from TD velocity data from the anteroseptum and posterior wall in the mid LV short-axis view.[58] Disadvantages of TD radial strain included signal noise without adequate image quality and the effect of the Doppler angle of incidence.

A more recent approach is application of a speckle-tracking program that is applied to routine gray-scale echocardiographic images, which is not limited by Doppler angle of incidence. Suffoletto et al studied 64 patients undergoing CRT.[54] Speckle tracking applied to routine midventricular short-axis images determines radial strain from multiple points averaged to 6 standard segments (Figure 8). Baseline speckle-tracking radial dyssynchrony (defined as a time difference in peak septal to posterior wall strain $\geq$ 130 milliseconds) predicted a significant increase in LV EF, with 89% sensitivity and 83% specific-

ity, in 50 patients followed up for 8 ± 5 months after CRT. An interesting subset of patients who did not have dyssynchrony by longitudinal TD velocities had a favorable response to CRT predicted by speckle-tracking radial dyssynchrony. These data suggest the additive value of assessing dyssynchrony from short-axis planes in addition to long-axis planes. A recent study of 176 patients combined longitudinal DTI velocity data with radial speckle-tracking strain data and found patients who had both positive longitudinal and radial dyssynchrony patterns had a high incidence of improvement in EF after CRT,[59] whereas patients with neither longitudinal nor radial dyssynchrony had a low incidence of EF improvement. Patients with heterogeneous patterns of dyssynchrony had intermediate responses. These data suggest that combining dyssynchrony data may be of additive value.[59]

THREE-DIMENSIONAL ECHOCARDIOGRAPHY

LV dyssynchrony in reality is a 3-dimensional phenomenon. Three-dimensional echocardiography provides a unique and powerful tool for the evaluation of LV dyssynchrony.[60] The advantage of real-time 3-dimensional echocardiography is that it allows for a comparison of synchrony between of the segments of the LV together in the same cardiac cycle (Figure 9). Regional wall-motion patterns can be visualized and quantified after segmentation of the LV chamber with semiautomatic contour tracing algorithms. Preliminary reports suggest that this approach enables a comprehensive analysis of LV wall motion before and during CRT with a direct comparison of endocardial wall motion between all LV segments. Kapetanakis et al calculated a systolic dyssynchrony index from the dispersion of time to minimum regional volume for all 16 LV segments and found this to be predictive of reverse remodeling after CRT in 26 patients.[61] This approach has the potential for a more comprehensive analysis of LV dyssynchrony.[62] However, disadvantages include lower spatial and temporal resolution, with frame rates for 3-dimensional wide-sector image acquisition at approximately 20 to 30 frames/s.

INTERVENTRICULAR DYSSYNCHRONY

Interventricular dyssynchrony, principally assessed as the interventricular mechanical delay (IVMD), is defined as the time difference between RV to LV ejection. This is determined as the time from the onset of the QRS to the onset of LV ejection versus RV ejection, usually measured as the onset of pulsed Doppler flow velocities in the LV and RV outflow tracts, respectively (Figure 10).[63-65] IVMD has been identified as a predictor of worsening symptom status and cardiac mortality in patients with heart failure, and has been shown to be of prognostic value in patients with CRT (usually >40-50 milliseconds).[65] Although IVMD is simple, reproducible, and possible with routine equipment,[15] it appears to be a nonspecific predictor of response to CRT. Bax et al demonstrated that IVMD was similar in 59 responders and 21 nonresponders to CRT: 47 ± 34 vs 49 ± 29 milliseconds, respectively (P = not significant).[16] Achilli et al reported results of the SCART study of 133 patients, where a positive response to CRT was predicted by IVMD longer than 44 milliseconds with a sensitivity of 66% and a specificity of 55%.[63] Richardson et al also showed that an IVMD longer than 50 milliseconds added prognostic information to patients undergoing CRT as part of the CARE-HF trial analysis.[65] The PROSPECT trial recently demonstrated that IVMD and other simple pulsed Doppler measures of dyssynchrony, such as the pre-ejection delay and the LV filling time to cardiac cycle length ratio, had the advantage of a high yield and high reproducibility in a multicenter setting.[18] However, most evidence suggests that interventricular dyssynchrony is not as useful in the prediction of response to CRT as LV intraventricular dyssynchrony, when a technically adequate study is possible. Comparisons of current principal measures of dyssynchrony appear in Table 2.

OTHER APPROACHES TO ASSESS DYSSYNCHRONY

Breithardt et al reported phase analysis using a semiautomatic method for endocardial border delineation.[66] The degree of LV dyssynchrony was quantified in 2D echocardiographic sequences from the apical 4-chamber view, focusing on the septal-lateral relationships. Computer-generated regional wall movement curves were compared by a mathematic phase analysis, based on Fourier transformation. The resulting septal-lateral phase angle difference is a quantitative measure for intraventricular dyssynchrony. Another method to determine dyssynchrony using conventional 2D echocardiography is velocity vector imaging. This method uses a series of unique B-mode pixel tracking algorithms to calculate regional myocardial velocities toward an operator-selected point of reference (Figure 11). A pilot study by Cannesson et al examined 23 patients with heart failure undergoing CRT using digital cineloops from standard apical views, with the user tracing the mid-LV wall from a single frame.[67] Dyssynchrony, defined as the greatest opposing wall peak longitudinal systolic velocity delay among the 3 views greater than or equal to 75 milliseconds, predicted EF response with 85% sensitivity and 80% specificity when patients were followed 8 ± 5 months after CRT.

EFFECTS ON LV REVERSE REMODELING AND MR

LV remodeling is a dynamic process characterized by progressive chamber dilatation, distortion of cavity shape, disruption of the mitral valve geometry with MR, and deterioration in contractile function that culminates in heart failure.[68,69] LV remodeling may be triggered by pressure or volume overload or loss of contracting myocytes from ischemic injury, or may be genetically programmed.[70] Although precise mechanisms and intracellular signaling pathways for LV remodeling are unknown, neurohormones and local trophic factors modulate the dynamic balance between distending forces that favor dilatation and the restraining forces imposed by the extracellular collagen matrix that may affect gene expression of myocyte function.[23] CRT often results in reverse remodeling where LV size and function progressively improve over time. This is a CRT-dependent, dynamic process where subsequent cessation of CRT results in progressive deterioration in LV function toward baseline values.[14] The extent of LV reverse remodeling varied according to cause of heart failure in the MIRACLE and other trials. Reduction in volume and severity of MR and the increase in EF were consistently 2- to 3-fold greater in nonischemic patients than in patients with ischemic heart failure in spite of significantly larger baseline volumes and lower EFs.[68] In an important study of 141 patients who received CRT, those who decreased LV end-systolic volume by at least 10% at 3 to 6 months had a more favorable long-term clinical outcome, including lower all-cause mortality (7% vs 31%), cardiovascular mortality (2% vs 24%), and heart failure events (12% vs 33%; all $P < .005$).[68,71]

CRT can reduce MR by improved temporal coordination of mechanical activation of the papillary muscles acutely and later

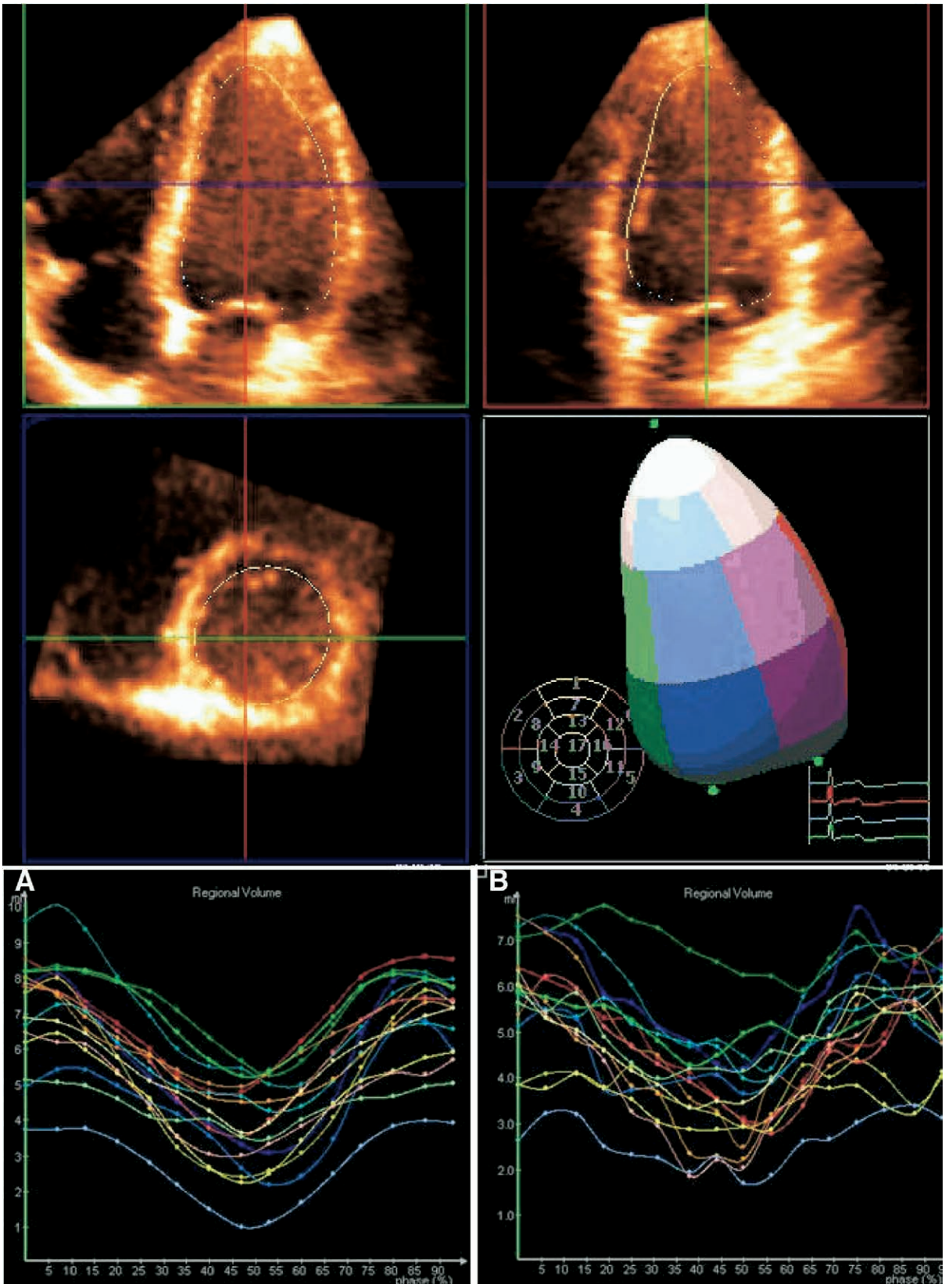

Figure 9 Three-dimensional echocardiographic assessment of segmental volume displacement in patient with normal synchrony (**A**) and with significant dyssynchrony (**B**).

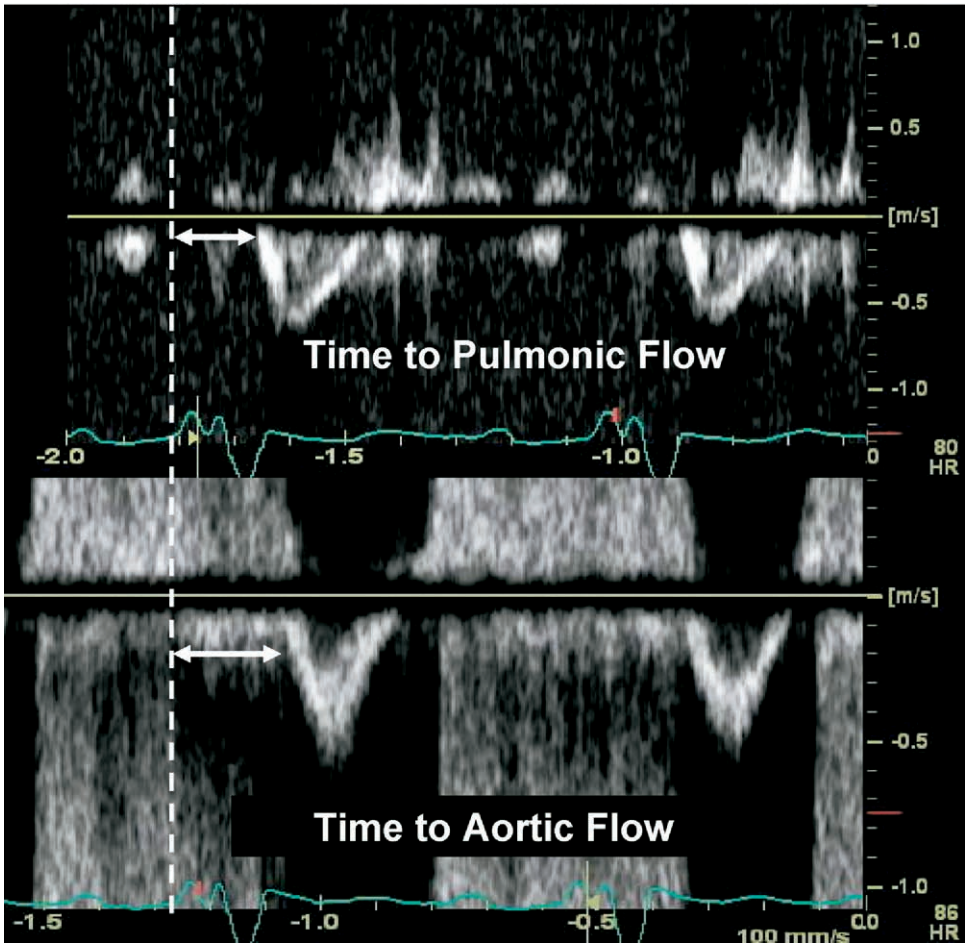

Figure 10 Pulsed Doppler from right ventricular outflow tract and left ventricular (LV) outflow tract demonstrating significant delay in LV ejection (>40 milliseconds).

improvements in LV size and geometry from reverse remodeling[28] (Figure 12). Breithardt et al used the proximal isovelocity surface area method during both pacing-off and CRT in the first week after CRT to report a significantly reduced regurgitant volume from 32 ± 19 to 19 ± 9 mL, and effective regurgitant orifice area from 25 ± 19 to 13 ± 8 mm^2, with CRT.[8] An important factor for acute reduction of MR after CRT appears to be improvement in the coordination of papillary muscle forces on the mitral chordae that increase the area of mitral leaflet coaptation. Kanzaki et al associated reductions in MR after CRT with acute improvements in the timing of mechanical activation of the papillary muscle sites, using mechanical strain activation mapping.[28]

PACING LEAD PLACEMENT

Several studies have suggested a potential role for echocardiographic Doppler methods to direct LV lead placement through identification of the anatomic site of latest mechanical activation. Ansalone et al were among the first to show that LV lead placement concordant with the site of latest velocity activation by TD was associated with a more favorable response to CRT.[30] They observed that the inferior or posterolateral wall was the location of latest mechanical activation in 75% of cases. Murphy et al demonstrated that the color-coded time-to-peak velocities approach described above could identify the site of latest systolic velocity and that lead placement at this site was associated with the greatest clinical and hemodynamic benefit of CRT.[72] There was a graduated response, such that LV pacing at a site one segment away from maximal delay was associated with a modest but more limited benefit, and patients paced at greater than one segment remote from the area of maximal delay had no significant reverse remodeling after a mean follow-up of more than 6 months. Suffoletto et al[54] utilized 2D speckle tracking to analyze LV radial strain to identify the site of latest mechanical activation before CRT and also observed that the patients with concordant LV lead placement had more favorable reverse remodeling. They found that 22 patients who had LV lead placement concordant with the site of latest activation had slightly greater improvements in LV EF (10 ± 5%), as compared with 24 patients who had discordant lead position (6 ± 5%; $P < .05$). Although these studies are encouraging, prospective studies will be needed to determine definitively the role of echocardiography in guiding LV lead placement.

RATIONALE FOR AV DELAY OPTIMIZATION

Because the ventricles are paced in CRT, the AV delay needs to be programmed. The optimal programmed AV delay for an electronic pacemaker has been defined as the AV delay that allows completion of the atrial contribution to diastolic filling resulting in most favorable

Table 2 Principal dyssynchrony indices associated with response to cardiac resynchronization therapy

Index	Method	Normal	Cutoff	Advantages	Disadvantages
Intraventricular longitudinal dyssynchrony					
Opposing wall delay, two sites[12,15,38]	Color tissue Doppler peak velocity (apical 4-chamber or long-axis views)	<50 ms	≥65 ms	Rapidly applied; offline analysis is possible	Requires color TD equipment; affected by passive motion tethering
Maximum wall delay, 12 sites[43,47]	Color tissue Doppler peak velocity (apical 4-chamber, 2-chamber, and long-axis views)	<90 ms	≥100 ms	More complete detection of longitudinal dyssynchrony; offline analysis is possible	Requires color TD equipment; affected by passive motion tethering
Yu index[14,31,43]	Color tissue Doppler, 12-segment SD (apical 4-chamber, 2-chamber, and long-axis views)	<30 ms	≥33 ms	More complete detection of longitudinal dyssynchrony; offline analysis is possible	Requires color TD equipment; more time-consuming; affected by passive motion tethering
Delay in onset of systolic velocity[51]	Pulsed tissue Doppler (apical 4-chamber, 2-chamber, and long-axis views; LV and RV)	<80 ms	≥100 ms	More widely available	Acquisition technically difficult; offline analysis is not possible; affected by passive motion tethering
Delayed longitudinal contraction[41,42]	Color tissue Doppler-strain-strain rate (apical views)	None	N/A	Less affected by passive motion or tethering; offline analysis is possible	Requires specialized color TD equipment; technically demanding
Intraventricular radial dyssynchrony					
Septal to posterior wall delay[34,35]	M-mode (parasternal mid-LV view)	<50 ms	≥130 ms	Widely available; rapidly applied; no advanced technical requirements	Largely affected by passive motion or tethering; difficulties with segmental akinesis
Septal to posterior wall delay[54,57]	Radial strain (parasternal mid-LV view)	<40 ms	≥130 ms	Less affected by passive motion or tethering; speckle tracking may be applied to routine images	Requires specialized instrumentation for analysis; assesses only radial dynamics
Interventricular dyssynchrony					
Interventricular mechanical delay[62-64]	Routine pulsed Doppler (RVOT and LVOT views)	<20 ms	≥40 ms	Widely available; no advanced technical requirements; highly reproducible	Nonspecific; affected by LV and RV function

LV, Left ventricular; *N/A*, not applicable; *OT*, outflow tract; *RV*, right ventricular; *TD*, tissue Doppler.

preload before ventricular contraction.[73] An AV delay programmed too short will result in absence or interruption of the atrial component (mitral A wave) by the premature ventricular contraction and closure of the mitral valve. An AV delay programmed too long can result in suboptimal LV preload or diastolic MR, or may even allow native LV conduction, which defeats the purpose of CRT.

Although the importance of AV synchrony is unquestioned, the need for routine echocardiographic Doppler AV timing optimization in all patients with CRT is controversial because an ideal approach has not yet been defined and there are often logistic challenges coordinating the echocardiography laboratory with electrophysiology technical staff for device programming. Auricchio et al concluded that although AV delay often positively impacts hemodynamics, LV resynchronization of intraventricular dyssynchrony is more important.[74] Many centers currently use empiric out-of-the-box AV delay device settings of approximately 100 to 130 milliseconds for CRT. Other centers rely on AV delay optimization algorithms based on ECG data to approximate the optimal AV delay optimal as [PR (ms) × 0.50], if QRS > 150 ms or [PR (ms) × 0.70], if QRS < 150 ms.[75] Sawhney et al recently conducted a prospective randomized trial of 40 patients comparing aortic Doppler optimized AV intervals to a fixed AV interval of 120 milliseconds after CRT.[76] AV optimized patients exhibited improved NYHA class and quality of life, but no significant improvement in 6-minute walk distance or EF at 3 months postimplant. A larger report of 215 patients undergoing Doppler-guided AV optimization found small differences between the baseline and post-AV optimization average AV delay (120 vs 135 milliseconds, respectively).[77] Furthermore, AV optimization enhanced LV hemodynamics in only a minority of patients with CRT, suggesting that a significant percentage of patients do not need to undergo formal AV optimization. Patients with intra-atrial conduction delay at baseline appeared to benefit greatest by prolonging the AV delays (150-250 milliseconds) during AV optimization (Figure 13).[77] These patients were identified by complete loss of the mitral inflow A wave

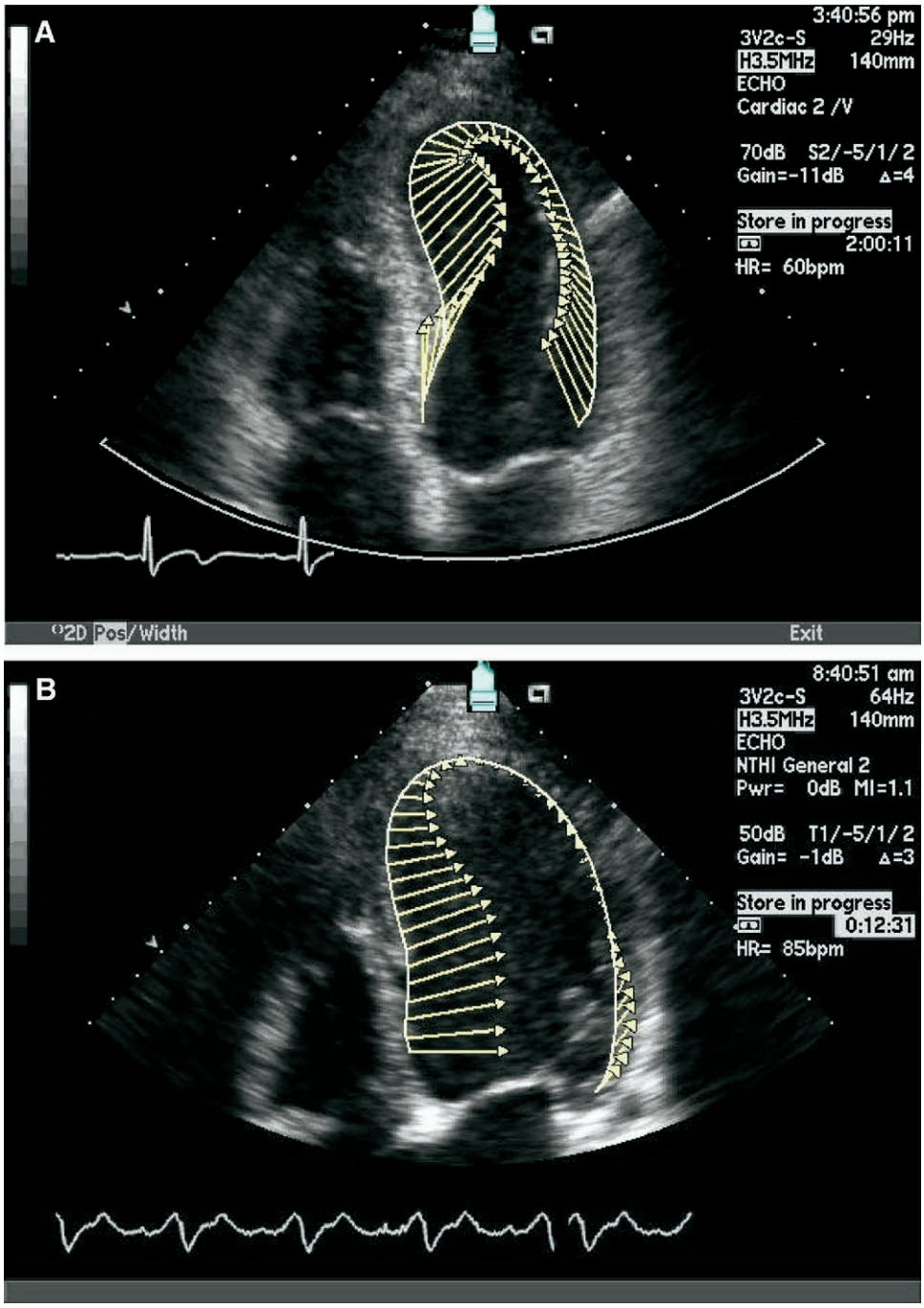

Figure 11 Velocity vector images demonstrating synchrony of velocity convergence toward center of left ventricle in healthy individual (**A**) and severe septal-lateral wall dyssynchrony in patient with heart failure and left bundle branch block (LBBB) referred for resynchronization therapy (**B**).

with an empiric setting that was too short. Although a recommendation for routine care has not been established, the following section provides guidelines for AV optimization after CRT.

RITTER AND ITERATIVE METHODS FOR AV DELAY OPTIMIZATION

Pulsed Doppler interrogation of mitral inflow to assess LV filling, and either pulsed Doppler or continuous wave Doppler sampling of the LV outflow tract to assess LV ejection, are utilized for the Ritter and iterative AV optimization protocols.[78,79] The method of Ritter et al attempted to optimally synchronize the termination of atrial contraction with the onset of ventricular systole.[79] This method requires programming the AV delay to a short (50 milliseconds) and then a long (200 or 250 milliseconds) interval while testing their impact on end-diastolic filling. The AV delay is then determined by correcting the long AV delay by the time shift from short and long Doppler tracings. The iterative method is simpler and begins by programming

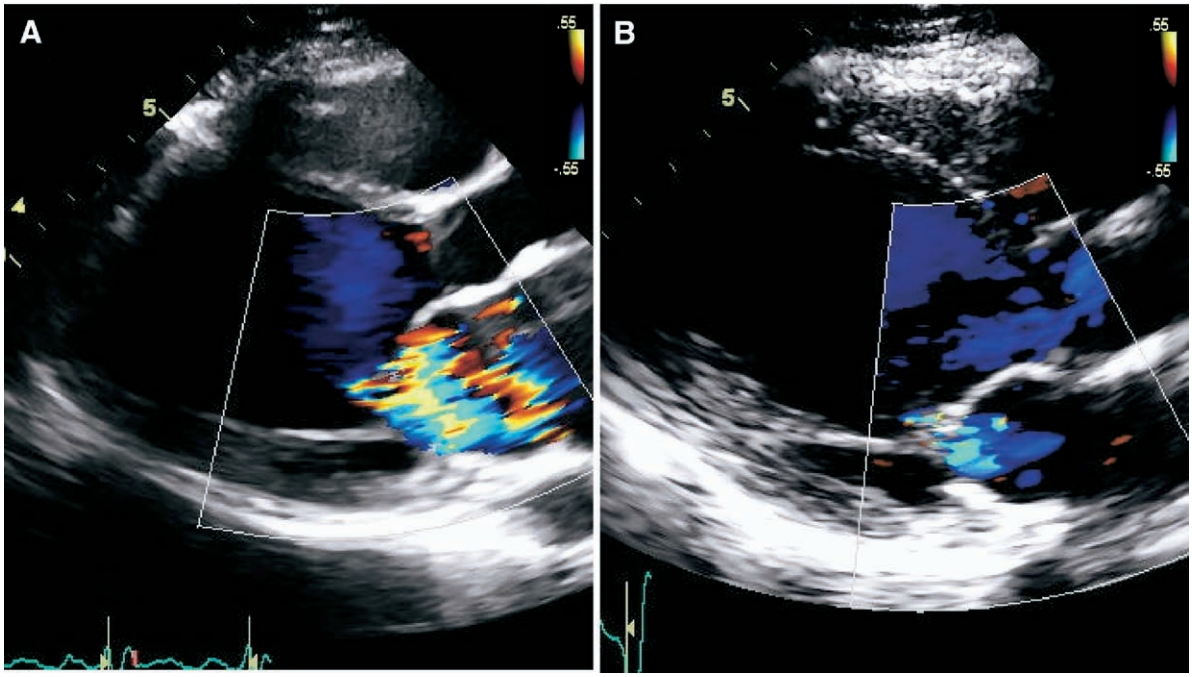

Figure 12 Parasternal long-axis view demonstrating reduction in mitral regurgitation in patient from before (**A**) to day after (**B**) resynchronization therapy.

the CRT device in atrial synchronous V pacing mode testing a series of AV intervals sequentially. This usually begins with an AV delay of 200 milliseconds, then decreases in increments of 20-millisecond intervals to a minimum AV delay as short as 60 milliseconds. The minimal AV delay that allows for adequate E and A wave separation and termination of the A wave at approximately 40 to 60 milliseconds before the onset of the QRS would be considered the optimal AV delay, and usually corresponds with a stage I diastolic filling pattern.[80] Technical features include positioning the pulsed wave sample volume deeper toward the left atrium (as opposed to the standard position at the mitral leaflet tips) to optimize detection of the mitral valve closure click, preparing settings of high sweep speeds and low filters, and inputting the ECG signal from the device directly to the ultrasound system, if possible. A variation on the iterative method for AV optimization uses transaortic Doppler velocities as a surrogate for stroke volume. The optimal sensed and paced AV delay is determined by the maximum aortic time-velocity integral value at 6 selected paced and sensed AV delays. A typical protocol will include measurements at AV delays of 60, 80, 100, 120, 140, and 160 milliseconds, with each paced and sensed AV delay setting separated by a rest period of at least 10 to 15 beats.

SIMPLIFIED DOPPLER SCREENING FOR AV OPTIMIZATION

A simplified Doppler screening protocol after CRT implantation is proposed using pulsed Doppler mitral inflow, because no consensus currently exists for the routine performance of AV optimization after CRT[77,81] (Figure 14).

Step 1: Optimize the ECG signal, including inverting the QRS complex if necessary.

Step 2: Optimize pulsed Doppler mitral inflow velocity using high sweep speeds, low filters, and the sample volume set at mitral annular level to determine closure clicks.

Step 3: Examine mitral inflow pattern. No AV optimization protocol is required if:

a. E and A waves are clearly identified and separated.
   and
b. Termination of the A wave occurs at least 40 milliseconds before QRS onset or mitral valve closure click.

Note that the mitral valve closure click should be aligned with the QRS complex as a surrogate for the beginning of LV systole. A pattern consistent with stage I diastolic filling (E wave lower than A wave) has not been shown to be improved on by AV alterations after CRT, and it is suggested by Kedia et al that formal AV optimization is not required in these patients.[77] AV optimization is recommended if any of the following are observed: A wave is not identified, E and A waves are merged, or A wave is truncated by mitral closure. AV optimization should be considered if stage II (pseudonormal) or stage III (restrictive) diastolic dysfunction is noted.[77,80] An absent A wave may be associated with intra-atrial conduction delay and often requires a longer AV pacing delay. On the other hand, E and A waves merge when the AV pacing delay is set too long. A truncated A wave requires lengthening of the AV delay. For these scenarios, either the iterative or Ritter methods described in detail above may be performed depending on the preference. Patients in atrial fibrillation or with frequent ventricular ectopy or tachycardia would not be appropriate candidates for AV optimization. Patients with mitral prosthetic valves may also be problematic.

BIVENTRICULAR (V-V) OPTIMIZATION

The recent generation of CRT devices allows for optimization of interventricular delays (V-V delays).[82-86] The first evidence of benefit from V-V optimization was reported by Sogaard et al.[87] The CRT settings were further optimized by V-V timing in 20 patients, resulting in an additional increase in LV EF (from 22 ± 6% at baseline to 30 ± 5% after CRT to 34 ± 6% after V-V optimization, $P < .01$). In

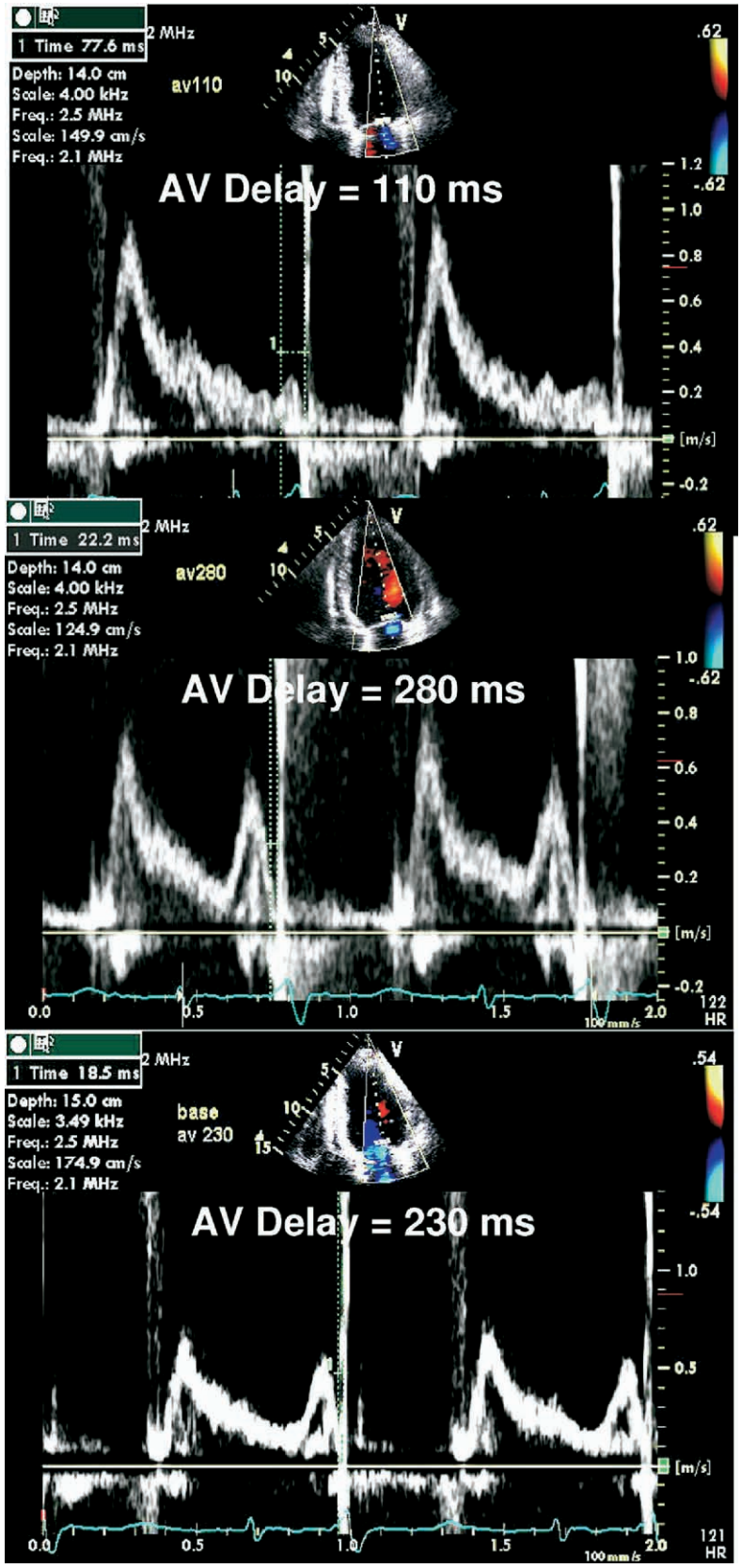

Figure 13 Atrioventricular optimization using mitral inflow velocities in patient with intra-atrial conduction delay. Default setting of 110 milliseconds resulted in loss of mitral inflow A wave (*top*). Delays of 280 milliseconds (*middle*) and 230 milliseconds (*bottom*) improved filling with contribution of atrial component. Alignment of mitral closure click with end of A wave was believed to be optimal with 230-millisecond delay.

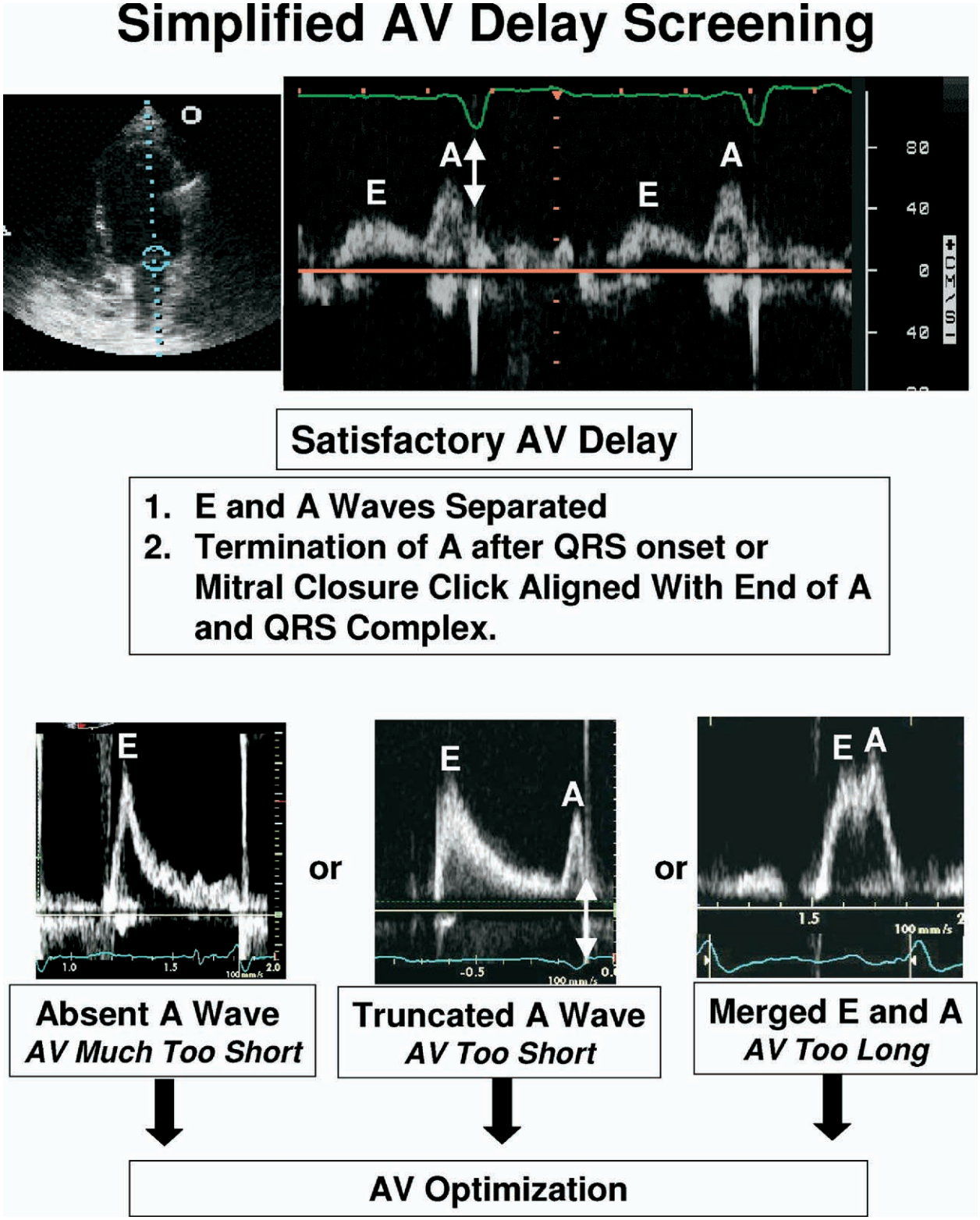

Figure 14 Simplified atrioventricular (AV) delay screening using mitral inflow Doppler velocities. Sample volume is placed within mitral valve to see closure click. AV optimization may not be necessary if E and A waves are separated, and termination of A wave is before QRS onset or mitral closure click aligned with end of A and QRS complex (usually type I diastolic dysfunction with E lower than A) (*top*). AV optimization is indicated if A wave is truncated, E and A waves are merged, or A wave is absent (*bottom*). Optimization may be considered if stage II (pseudonormal) or stage III (restrictive) diastolic filling patterns are present.

addition, Bordachar et al demonstrated that V-V optimization resulted in a significant reduction in MR.[88,89] V-V optimization is generally performed by changing the V-V sequence, starting with the LV being activated before the RV, and then stepwise lengthening or shortening of the V-V interval (eg, with intervals of 20 milliseconds) and measuring the highest aortic time-velocity integral. Current studies have shown that subsets of patients do acutely benefit from V-V optimization, but long-term benefit has yet to be determined.

DYSSYNCHRONY IN THE NARROW QRS PATIENT POPULATION

Mechanical dyssynchrony may exist in a subset of patients with heart failure who have narrow QRS duration (<120 milliseconds). If CRT can be shown to be of benefit to these patients, the application of echocardiographic assessment of dyssynchrony is potentially of great importance for patient selection for therapy.[20,21,64] Bleeker et al showed CRT to benefit 33 patients with NYHA class III/VI heart failure and EF less than or equal to 35%, but QRS less than 120 milliseconds, who had mechanical dyssynchrony defined as a septal-to-lateral wall time-to-peak systolic velocity delay of greater than or equal to 65 milliseconds by TD.[90] In a separate study, Yu et al reported results on 51 patients with heart failure with narrow QRS (<120 milliseconds) who had CRT based on TD measures of dyssynchrony. CRT resulted in significant reductions of LV end-systolic volume, and improvement of NYHA class, 6-minute hall-walk distance, and EF, similar to patients with wide QRS who underwent CRT.[91] The first randomized trial of CRT in patients with heart failure with narrow QRS complexes (<130 milliseconds), known as the RethinQ trial, was recently published by Beshai et al.[92] Dyssynchrony was defined as a TD septal-to-lateral wall cutoff of greater than or equal to 65 milliseconds from either apical 4-chamber views or apical long-axis views, or M-mode septal to posterior wall delay greater than or equal to 130 milliseconds. All patients who met inclusion criteria (96% by TD) had CRT devices implanted, and 172 were randomized to either CRT-off as a control or CRT-on. This trial failed to show a therapeutic effect of CRT on the primary end point of peak myocardial oxygen consumption. Although a positive effect of CRT was observed on the secondary end point of improvement in NYHA functional class, other parameters including quality-of-life score, 6-minute walk test, and LV reverse remodeling did not change. Benefit of CRT on 6-minute walk distance, however, was demonstrated in patients with nonischemic disease. A prespecified subgroup analysis of patients with borderline QRS duration between 120 and 130 milliseconds and dyssynchrony showed benefit of CRT by significantly improving their peak myocardial oxygen consumption and NYHA functional class.[92] In summary, the RethinQ randomized trial concluded as mostly negative, however, many unanswered questions remain. It is unclear whether the type or degree of dyssynchrony may be refined in this narrow QRS population to predict response to CRT, or whether other patient selection factors may impact results. Clearly, future larger randomized clinical trials are required to determine the role of CRT in patients with narrow QRS, and the potential pivotal role that echocardiographic Doppler will play in their selection for therapy.

APPLICATION OF DYSSYNCHRONY ANALYSIS IN CLINICAL PRACTICE AND REPORTING

Although a number of echocardiographic dyssynchrony methods discussed have suggested superiority to ECG QRS width for predicting response to CRT, evidence from large-scale clinical trials and current practice guidelines do not include an echocardiographic Doppler dyssynchrony study for patient selection.[13] **Accordingly, this writing group currently does not recommend that patients who meet accepted criteria for CRT should have therapy withheld because of results of an echocardiographic Doppler dyssynchrony study**.[13]

We acknowledge that many centers are currently applying these analyses as an adjunct to assist with clinical decision making for CRT for selected patients who may have borderline inclusion criteria, such as a borderline QRS duration. Although limited data are available from clinical trials, enrollment in the CARE-HF randomized CRT trial required patients with borderline QRS duration between 120 and 149 milliseconds to meet two of 3 additional criteria for dyssynchrony: an aortic pre-ejection delay longer than 140 milliseconds, an IVMD longer than 40 milliseconds, or delayed activation of the posterolateral LV wall.[6] In addition, the subgroup analysis of patients with QRS 120 to 129 milliseconds and evidence of mechanical dyssynchrony in RethinQ demonstrated benefit from CRT.[92] Other possible clinical settings where dyssynchrony analysis may potentially play a role is in patients with borderline EF or ambiguous clinical histories for NYHA functional class. If there is a clinical request for a dyssynchrony echocardiogram for these or other scenarios, it is the consensus of this group that it is reasonable for the following dyssynchrony measures to be performed and reported.

TD Opposing Wall Delay (the Maximum Time from S Wave Peak of One Wall to the S Wave Peak of the Opposing Wall) in Apical 4-chamber or Apical Long-axis Views

A cutoff of greater than or equal to 65 milliseconds is consistent with significant dyssynchrony, or Yu index (12-site SD) using longitudinal TD velocities from 3 standard apical views. A cutoff of greater than or equal to 33 milliseconds is consistent with significant dyssynchrony.

IVMD Using Pulsed Doppler from RV Outflow Tracts and LV Outflow Tracts

A cutoff of greater than or equal to 40 milliseconds is consistent with significant dyssynchrony.

Radial Dynamics, Which May be Additive Value, Include Septal-to-Posterior Wall Delay Using M-Mode in Patients With Non-Ischemic Disease With Technically High Quality Data, Or Using Speckle Tracking Radial Strain

A cutoff of greater than or equal to 130 milliseconds is consistent with significant dyssynchrony.

Other indices that appear in Table 2 may be included, if desired by individual laboratories. A conservative approach to carefully exclude mechanical dyssynchrony is advised, because an optimal approach has not yet been clearly defined. Agreement with more than one of these measures improves the confidence in the dyssynchrony analysis,[59] although a precise scheme to their collective additive value is currently unknown. **We advise that the dyssynchrony reporting should not include a recommendation whether a patient should undergo CRT, as this should be a clinical decision on a case-by-case basis for these borderline or**

challenging cases. Many other methods described in this report are promising, but may currently be too technically challenging or underdeveloped.

Echocardiography plays an exciting and evolving role in the care of the patient with CRT, from quantifying improvements in ventricular function and MR to optimizing the device after implantation. Although a great deal of work has been done to quantify mechanical dyssynchrony in hopes of refining patient selection and guiding lead placement, this is a complex and challenging field with future work needed and several promising studies ongoing. Technologic improvements in echocardiographic data acquisition and analysis as well as advances in our understanding of the pathophysiology of dyssynchrony and CRT have great potential to impact future clinical practice and improve patient outcome.

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