

**Minicorso sulla CSP: PARTE III – CSP avanzata,
popolazioni specialie scenari futuri**

LBBAP nei ritardi di conduzione intraventricolare aspecifici(NIVCD)

RADMILOVIC JURI



LBBAP: Left bundle Branch Area Pacing

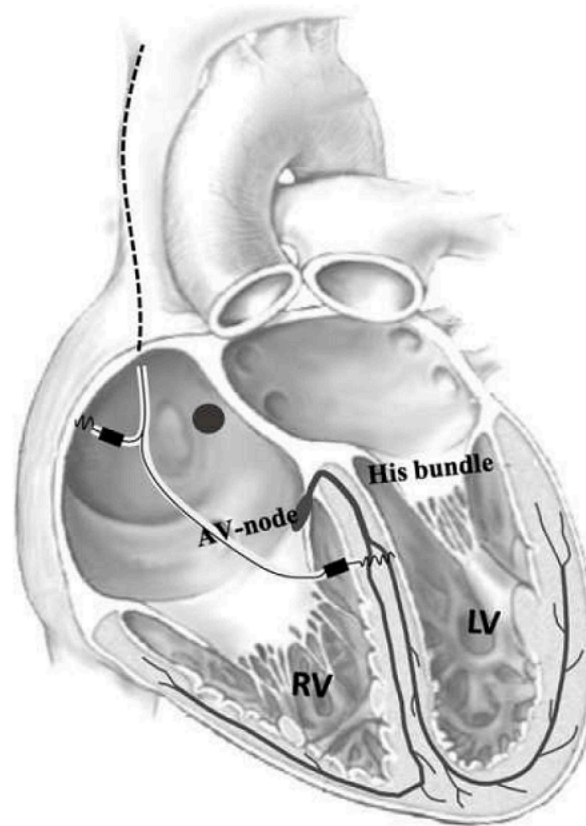
Stimolazione cardiaca fisiologica dell'area della branca sinistra

NIVCD: Non-Specific Intraventricular Conduction Delay

Ritardo di conduzione intraventricolare aspecifico

Nei pazienti con NIVCD, la classica terapia di resincronizzazione cardiaca CRT è spesso meno efficace

Vantaggio di stimolare direttamente il sistema di conduzione, correggendo o migliorando l'asincronia cardiaca



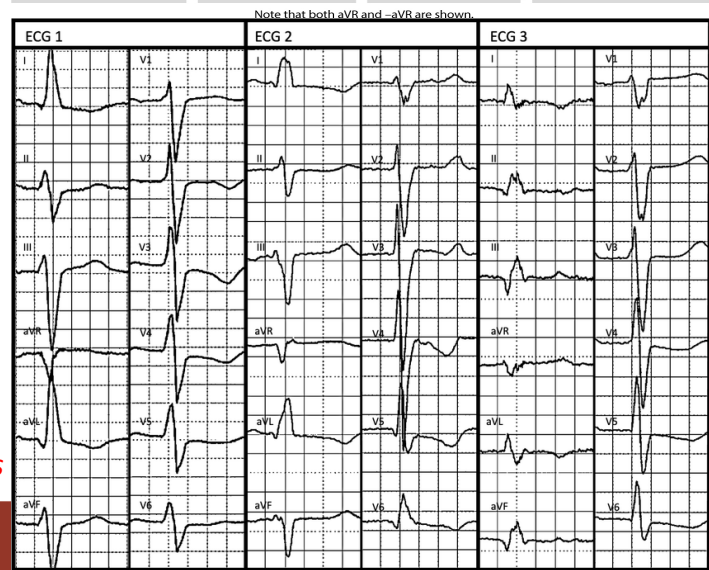
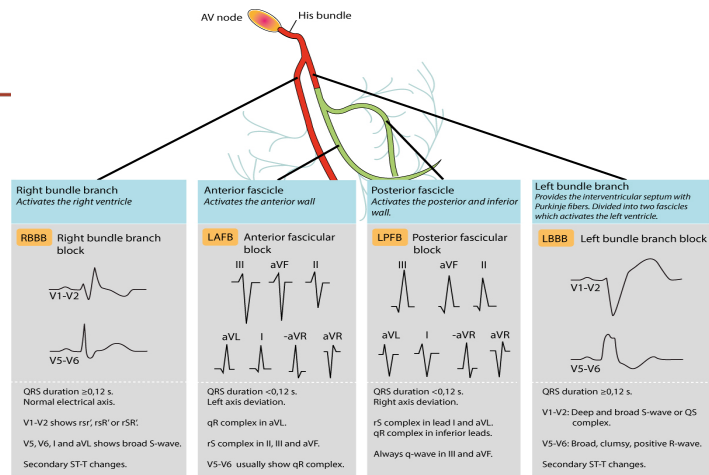
Vijayaraman P, Ponnusamy S, Cano O, et al. Left bundle branch area pacing for cardiac resynchronization therapy: results from the International LBBAP Collaborative Study Group. JACC Clin Electrophysiol 2021; 7:135–147.



NIVCD: Non-Specific Intraventricular Conduction Delay

Ritardo di conduzione intraventricolare aspecifico
Rallentamento del passaggio dell'impulso elettrico intraventricolare, causa di dissincronia nella contrattilità e compromissione della funzione sistolica

Aspecifico in quanto il complesso QRS è allungato (solitamente >120 ms), in assenza dei classici criteri del blocco di branca destro o sinistro



NIVCD examples

Il Ruolo della LBBAP

1. Ripristino dell'Asincronia: La LBBAP posiziona un elettrocatteter in profondità nel setto interventricolare per "catturare" la branca sinistra o il suo fascio prossimale. Questo permette all'impulso di propagarsi attraverso le vie naturali del cuore, riducendo la durata del QRS e migliorando l'efficienza di pompa.

2. Alternativa alla CRT: Nei pazienti con ritardi di conduzione ampi (in genere $QRS > 130-150$ ms) e disfunzione ventricolare, la terapia di resincronizzazione cardiaca (CRT) tradizionale prevede l'uso di un catetere nel seno coronarico.

LBBAP si sta affermando come un'alternativa più fisiologica, spesso in grado di garantire un restringimento del QRS superiore rispetto alla biventricolare classica.

3. Selezione del Paziente: L'indicazione clinica e l'efficacia dipendono fortemente dall'estensione della fibrosi miocardica. Se il ritardo è dovuto a una malattia diffusa delle diramazioni periferiche del sistema di conduzione, la correzione può essere solo parziale.

Probability of CRT Response According to QRS Duration

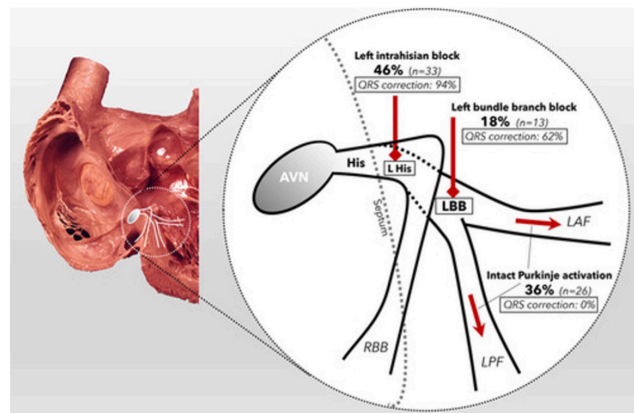
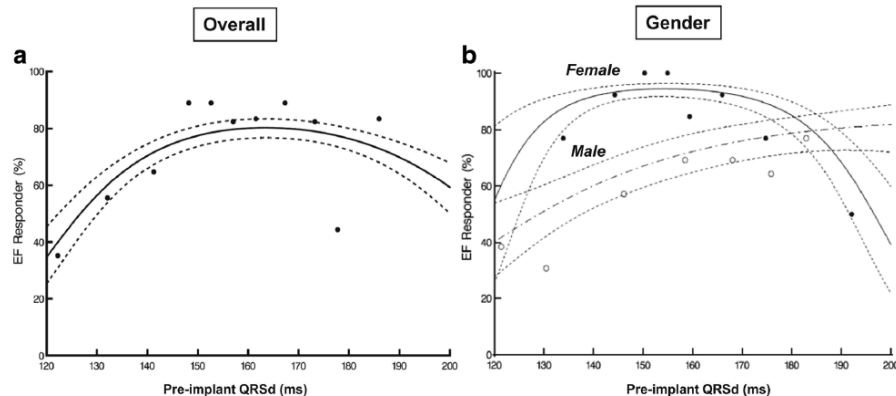


FIGURE 4
Schematic of the proximal conduction system, demonstrating the prevalence of each form of conduction disorder within the cohort (bold) and the percentage of patients whose QRSd was corrected by HBP (italic). Reproduced from reference 68, Upadhyay et al., with permission.

Vijayaraman P, Ponnusamy S, Cano O, et al. Left bundle branch area pacing for cardiac resynchronization therapy: results from the International LBBAP Collaborative Study Group. *JACC Clin Electrophysiol* 2021; 7:135–147.



Failure of BIV-CRT

CRT non responders represent between 30% and 50% of CRT patients

Pre-implant

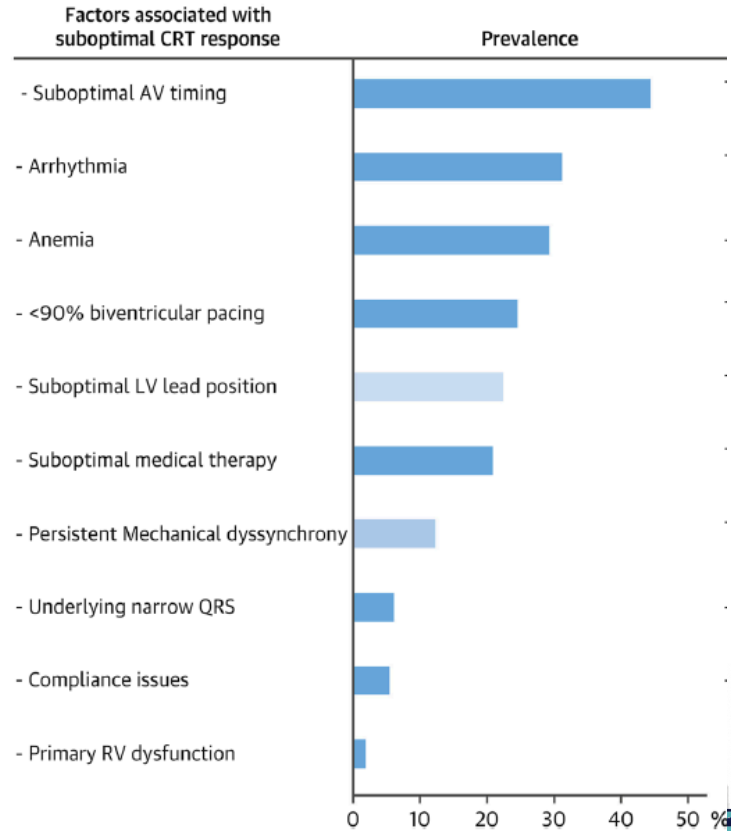
- Patient selection: symptomatic heart failure – impaired LV function - ventricular dyssynchrony
- ECG morphology: LBBB (best response) – RBBB/IVCD (atypical electrical activation – reduced response)
- Ischemic etiology and myocardial scar
- Atrial fibrillation (around 25%)

Peri-implant

- Stimulation site: anatomy of cardiac veins - lateral/postero-lateral veins with lateral free wall as best stimulation target
- LV lead technology: multipoint pacing

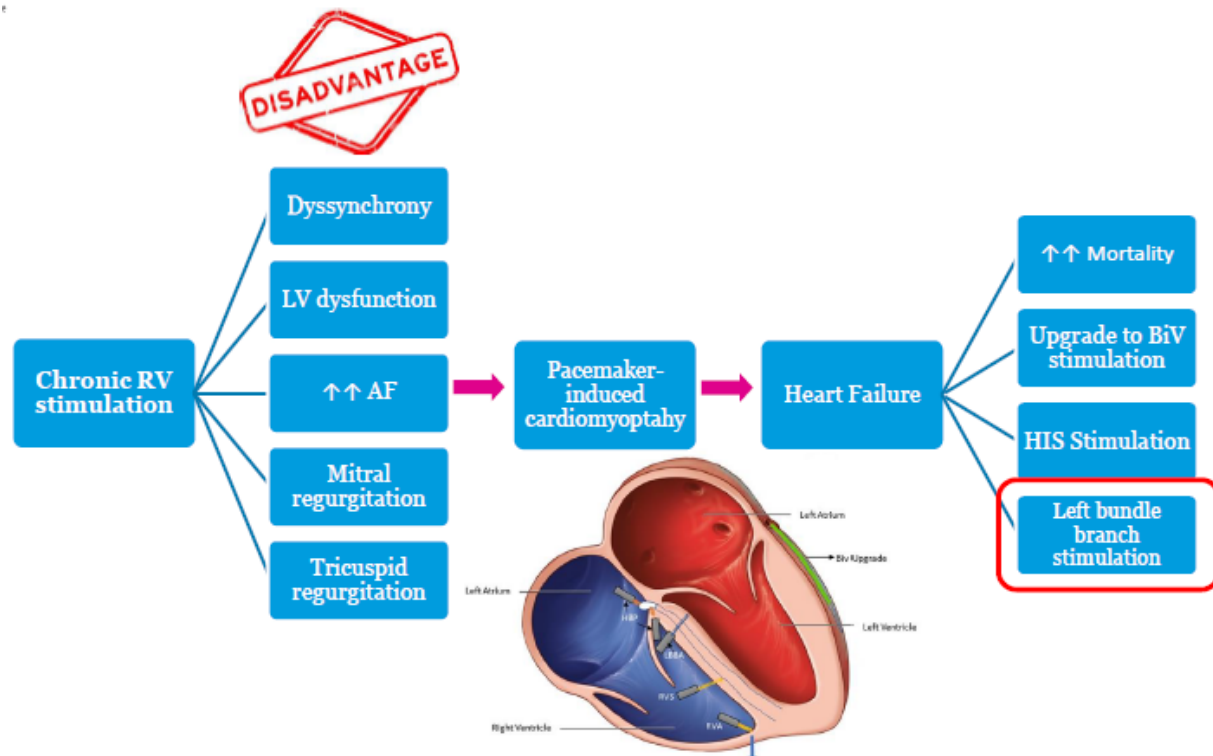
Post-implant

- Biventricular pacing burden: catheter ablation – antiarrhythmic drugs
- Programming and optimization: AV – VV intervals (optimal diastolic filling of LV)



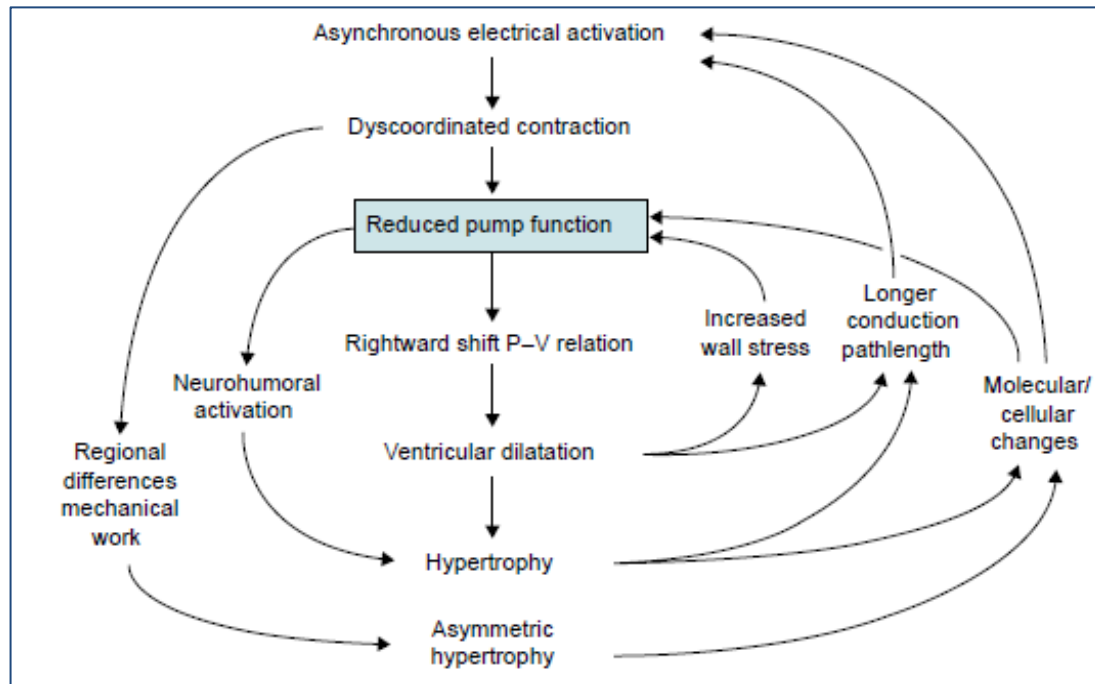
Jastrzebski M, Wilinski J, Fijorek K, Sondej T, Czarnecka D. Mortality and morbidity in cardiac resynchronization on patients: impact of lead position, paced left ventricular QRS morphology and other characteristics on long-term outcome. Europace 2013;15:258–265.

La stimolazione fisiologica: quando?



Tasneem Z Naqvi et. al. Adverse effects of right ventricular pacing on cardiac function: prevalence, prevention and treatment with physiologic pacing





Relationship between asynchronous ventricular activation leading to reduced pump function. P–V, pressure volume

Vernooy K, Verbeek XA, Peschar M, Prinzen FW. Relation between abnormal ventricular impulse conduction and heart failure. *J Interv Cardiol* 2003;16:557–62.



MELOS — MULTICENTER EUROPEAN LEFT BUNDLE BRANCH AREA PACING OUTCOMES STUDY



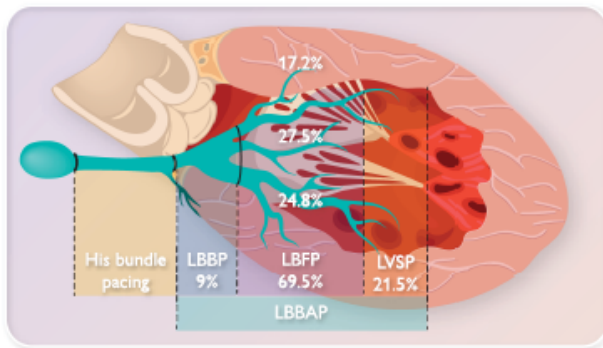
Prospective, multicenter,
registry-based observational study



2533
Participants



14
European centres



Independent predictors of LBBAP lead implantation failure

Heart failure indication	OR 1.49, 95% CI 1.01–2.21
Baseline QRS duration, per 10 ms	OR 1.08, 95% CI 1.03–1.14
LVEDD, per 10 mm increase	OR 1.53, 95% CI 1.26–1.86

LBBAP implantation success

Bradycardia indication success	92.4%
Heart failure indication success	82.2%

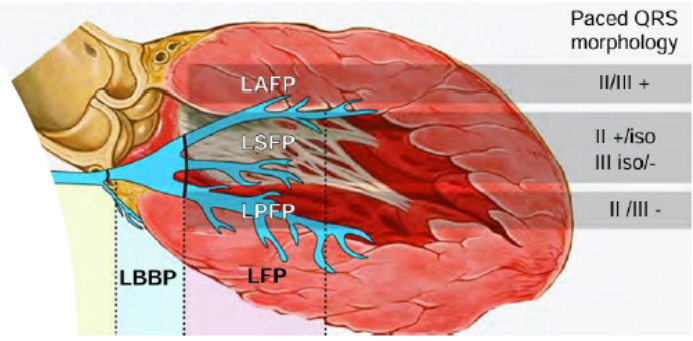
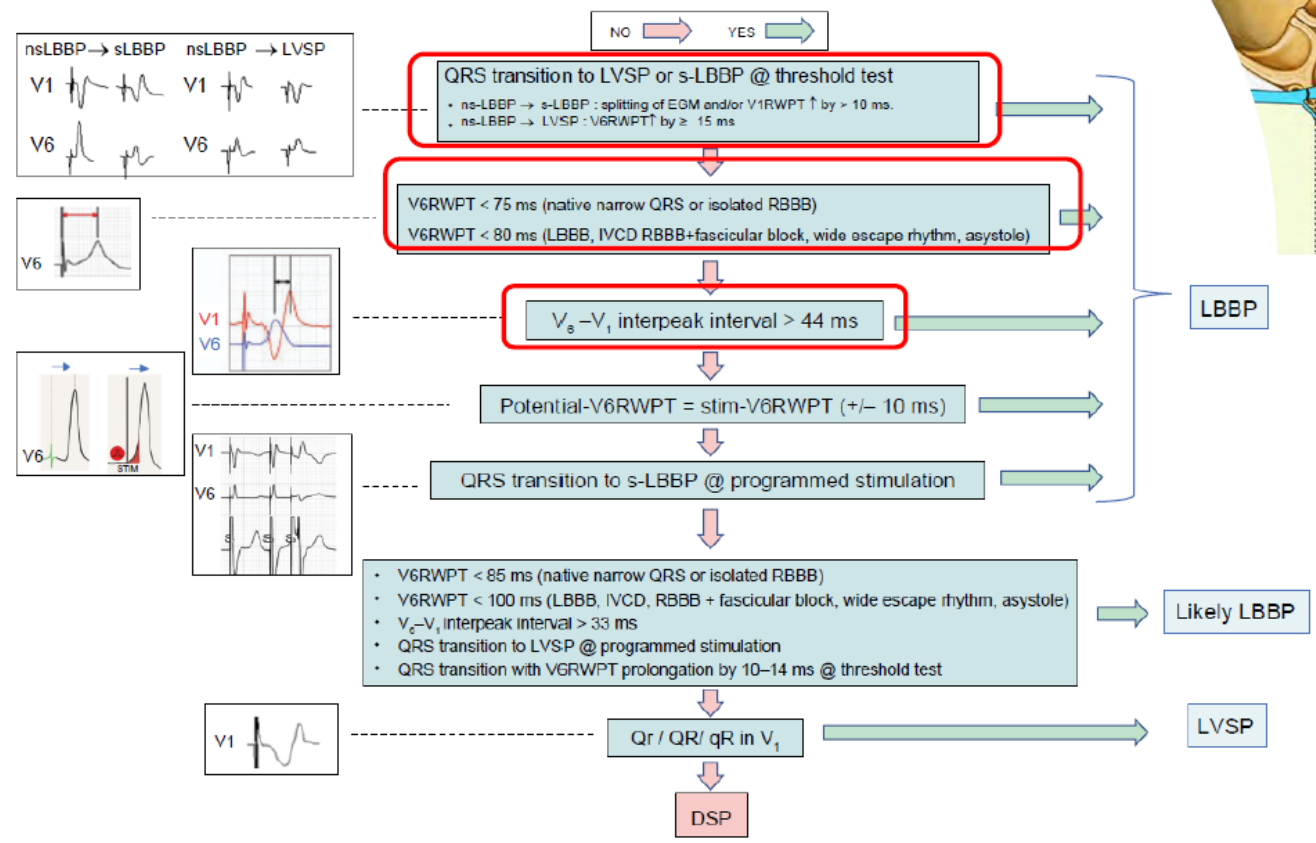
LBBAP lead complications

• Acute perforation to LV	8.3%
• Lead dislodgement	3.7%
• Acute chest pain	1.5%
• Capture threshold rise	1.0%
• Acute coronary syndrome	0.7%
• Trapped/damaged helix	0.4%
• Delayed perforation to LV	0.4%
• Other	0.1%

*Left bundle branch area
pacing outcomes: the
multicentre European
MELOS study Open Access
Marek Jastrzębski et al.
European Heart Journal,
Volume 43, Issue 40, 21
October 2022, Pages 4161–
4173*



LBBAP criteria

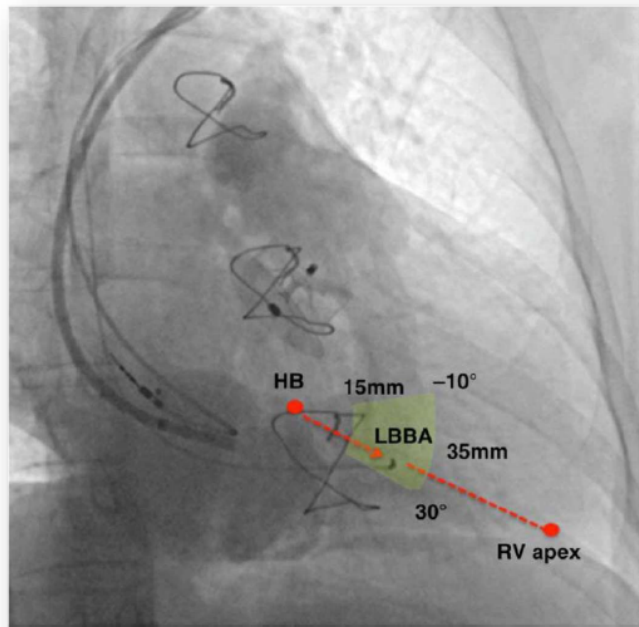


Paced QRS morphology
II/III +
II +/-iso
III iso/-
II /III -

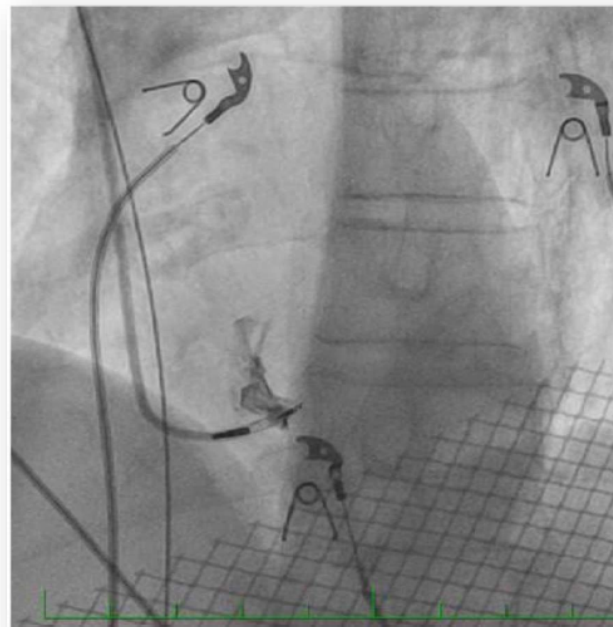
LBBAP Proiezioni

Nella **stimolazione della branca sinistra** il sito di stimolazione è situato nel fascio interventricolare più in basso del fascio di His e a valle del blocco di conduzione. Con LBBAP si ha la possibilità di **superare il blocco di conduzione, correggere il disturbo di conduzione IV e migliorare il sincronismo biventricolare.**

RAO



LAO



2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

Developed by the Task Force on cardiac pacing and cardiac resynchronization therapy of the European Society of Cardiology (ESC)

Patients with HF and non-LBBB present a significant challenge in clinical practice, as data from large BiV-CRT clinical trials do not indicate favourable outcomes for these patients.

BiVP should be considered for patients with non-LBBB and a QRS duration >150 ms, and a Class IIb recommendation for those with a QRS duration of 130–150 ms, without any indication for CSP

LBBB QRS morphology

CRT is recommended for symptomatic patients with HF in SR with LVEF $\leq 35\%$, QRS duration ≥ 150 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.^{37,39,40,254–266,283,284}

I

A

CRT should be considered for symptomatic patients with HF in SR with LVEF $\leq 35\%$, QRS duration 130–149 ms, and LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity and mortality.^{37,39,40,254–266,283,284}

IIa

B

Non-LBBB QRS morphology

CRT should be considered for symptomatic patients with HF in SR with LVEF $\leq 35\%$, QRS duration ≥ 150 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.^{37,39,40,254–266,283,284}

IIa

B

CRT may be considered for symptomatic patients with HF in SR with LVEF $\leq 35\%$, QRS duration 130–149 ms, and non-LBBB QRS morphology despite OMT, in order to improve symptoms and reduce morbidity.^{273–278,281}

IIb

B

QRS duration

CRT is not indicated in patients with HF and QRS duration <130 ms without an indication for RV pacing.^{264,282}

III

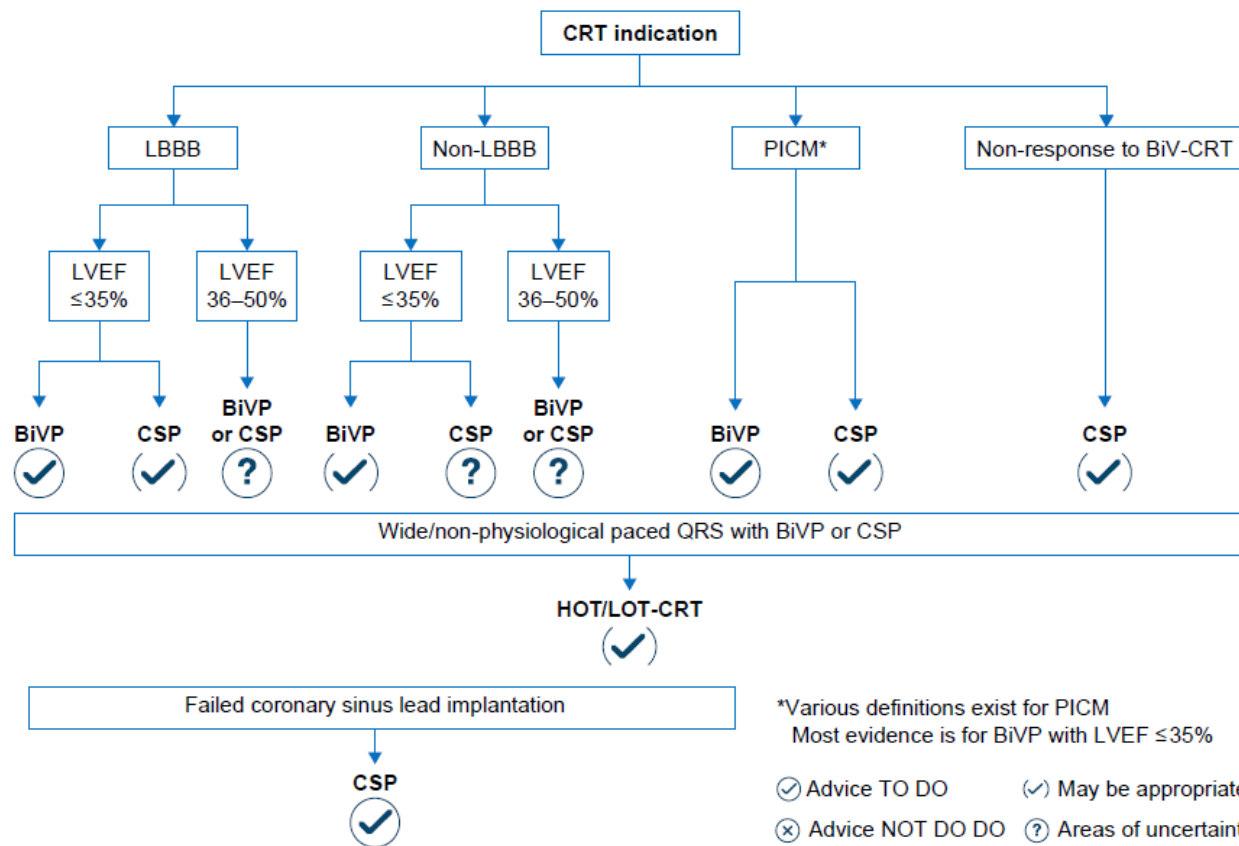
A

2023 HRS/APHRS/LAHRs guidelines attribute a Class 2b indication for CSP in patients with non-LBBB with NYHA III–IV + QRS 120–149 ms, as well as NYHA II + QRS ≥ 150 ms

Recommendations for non-LBBB, sinus rhythm, QRS duration ≥ 150 ms, NYHA class II–IV symptoms		
COR	LOE	Recommendations
2a	A	1. In patients who have LVEF $\leq 35\%$, sinus rhythm, a non-LBBB pattern with QRS duration ≥ 150 ms, and NYHA class III or ambulatory class IV symptoms on GDMT, CRT with BiV pacing can be useful to improve functional class, cardiac structure, and LVEF.
2b	B-R (CRT)	2. In patients who have LVEF $\leq 35\%$, sinus rhythm, a non-LBBB pattern with QRS duration ≥ 150 ms, and NYHA class II symptoms on GDMT, CPP may be considered to potentially improve mortality, HFH, LVEF, and/or functional class.
	C-LD (HBP, LBBAP)	
2b	C-LD	3. In patients with LVEF $\leq 35\%$, sinus rhythm, non-LBBB with QRS duration ≥ 150 ms, and NYHA class II–IV symptoms on GDMT, CSP with HBP or LBBAP may be reasonable if effective CRT cannot be achieved with BiV pacing based on anatomical or functional criteria.
2b	B-NR (CRT)	1. In patients who have LVEF $\leq 35\%$, sinus rhythm, a non-LBBB pattern with QRS duration 120–149 ms, and NYHA class III or IV symptoms on GDMT, the usefulness of CPP is not well established.
	C-LD (HBP, LBBAP)	

*2023 HRS/APHRS/LAHRs
Guideline on Cardiac
Physiologic Pacing*





European Society of Cardiology (ESC) clinical consensus statement on indications for conduction system pacing, with special contribution of the European Heart Rhythm Association of the ESC and endorsed by the Asia Pacific Heart Rhythm Society, the Canadian Heart Rhythm Society, the Heart Rhythm Society, and the Latin American Heart Rhythm Society
Michael Glikson, et al. EP Europace, Volume 27, Issue 4, April 2025



Advice: CSP-CRT

Strength of evidence

Advice TO DO

In candidates for BiVP in whom coronary sinus lead implantation is unsuccessful, CSP is advised as rescue therapy.



May be appropriate TO DO

For patients with LVEF $\leq 35\%$, LBBB with QRS ≥ 130 ms, and Class II–IV HF symptoms despite GDMT, CSP may be appropriate as an alternative to BiVP to improve LVEF, exercise capacity, and symptoms and to reduce HFH.



In non-responders to BiV-CRT, it may be appropriate to implant CSP to improve HF symptoms and LVEF.



>90% agree

In the presence of specific patient populations where a simpler device is desired (e.g. frail patients, patients with limited life expectancy, or those requiring a smaller device), it may be appropriate to choose CSP instead of BiVP as a primary strategy, taking into account operator experience.



>90% agree

Areas of uncertainty

For patients with a CRT indication and non-LBBB, the clinical impact of CSP is uncertain.



>90% agree

For patients with HF and LVEF $> 35\%$ without an indication for ventricular pacing, the clinical impact of CSP is uncertain.



>90% agree

European Society of Cardiology (ESC) clinical consensus statement on indications for conduction system pacing, with special contribution of the European Heart Rhythm Association of the ESC and endorsed by the Asia Pacific Heart Rhythm Society, the Canadian Heart Rhythm Society, the Heart Rhythm Society, and the Latin American Heart Rhythm Society
Michael Glikson, et al. EP Europace, Volume 27, Issue 4, April 2025



The number of patients with non-specific intra-ventricular conduction delay (NIVCD) who have been studied with LBBAP is very small, and treatment efficacy in this patient subgroup has not been reported separately.

Vijayaraman P, Ponnusamy S, Cano O, Sharma PS, Naperkowski A, Subposh FA *et al.* Left bundle branch area pacing for cardiac resynchronization therapy: results from the international LBBAP collaborative study group. *JACC Clin Electrophysiol* 2021;**7**:135–47.

No randomized trial has yet assessed the benefit of CSP-CRT compared with BiV-CRT in this population, and further studies are needed to establish its advantages.

Friedman DJ, Al-Khatib SM, Dalgaard F, Fudim M, Abraham WT, Cleland JGF *et al.* Cardiac resynchronization therapy improves outcomes in patients with intraventricular conduction delay but not right bundle branch block: a patient-level meta-analysis of randomized controlled trials. *Circulation* 2023;**147**:812–23.

Observational data on LBBAP combined with coronary sinus pacing, known as left bundle branch-optimized CRT (LOT-CRT), have shown encouraging results in patients with NIVCD and are discussed later

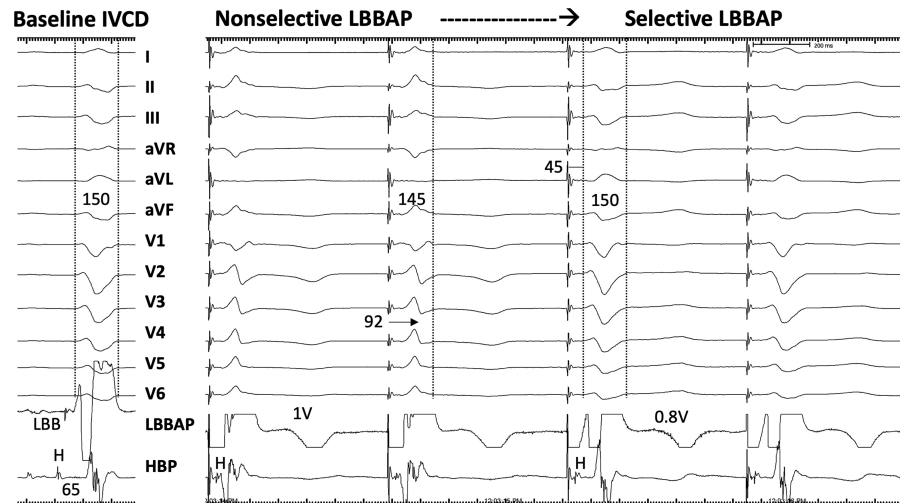
Chen X, Li X, Bai Y, Wang J, Qin S, Bai J *et al.* Electrical resynchronization and clinical outcomes during long-term follow-up in intraventricular conduction delay patients applied left bundle branch pacing-optimized cardiac resynchronization therapy. *Circ Arrhythm Electrophysiol* 2023;**16**:e011761.



Recent small non randomized studies assessed the use of CSP among patients with CHF, non-LBBB, QRS duration >150 ms, NYHA class II–IV symptoms

103 of 325 patients who were treated with LBBAP for CRT indication had a non-LBBB QRS pattern.

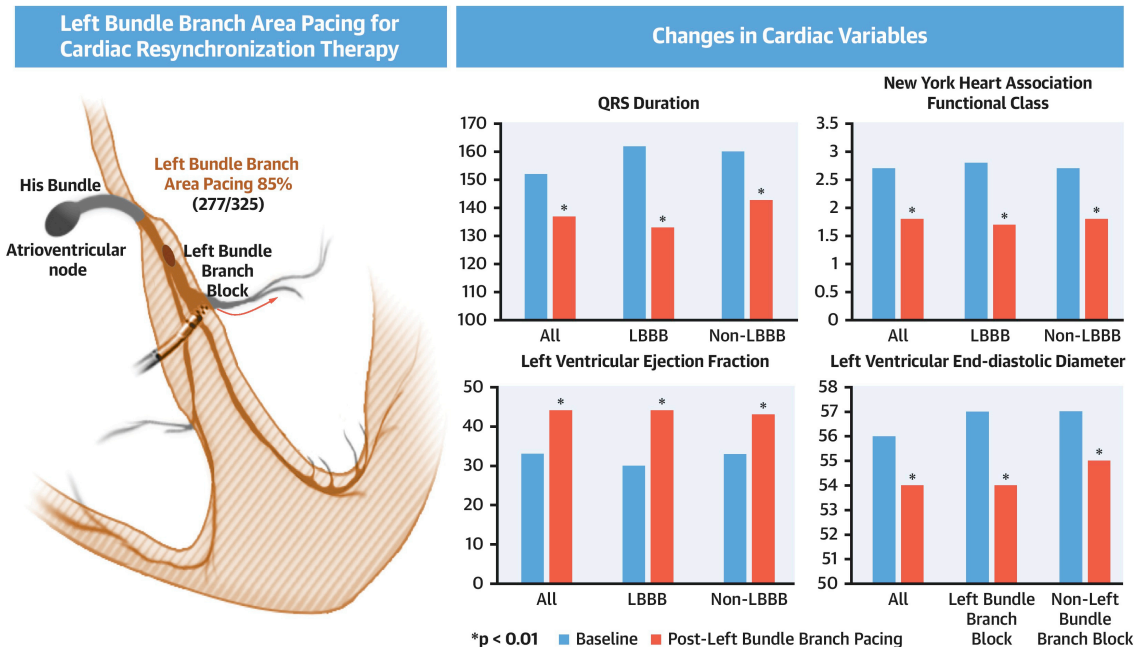
Patients experienced significant narrowing of the QRS duration (160 ± 28 to 143 ± 23 ms), improvement in LVEF ($33\% \pm 0.1\%$ to $43\% \pm 0.12\%$), and improvement in NYHA class (average class 2.7 ± 0.7 to 1.8 ± 0.6)



Vijayaraman P, Ponnusamy S, Cano O, et al. Left bundle branch area pacing for cardiac resynchronization therapy: results from the International LBBAP Collaborative Study Group. *JACC Clin Electrophysiol* 2021;7:135–147



CENTRAL ILLUSTRATION: Left Bundle Branch Area Pacing for Cardiac Resynchronization Therapy



Vijayaraman, P. et al. J Am Coll Cardiol EP. 2021;7(2):135-47.

LBBAP resulted in significant reductions in QRS duration, New York Heart Association functional class, and left ventricular (LV) end-diastolic diameter along with significant improvement in LV ejection fraction in patients with left bundle branch block (LBBB) and non-LBBB

Vijayaraman P, Ponnusamy S, Cano O, et al. Left bundle branch area pacing for cardiac resynchronization therapy: results from the International LBBAP Collaborative Study Group. JACC Clin Electrophysiol 2021;7:135-147



LBBAP may be a reasonable alternative for patients with LV dysfunction and RBBB. Future randomized studies are essential to understand the role of LBBAP in this patient population (Vijayaraman et al.).

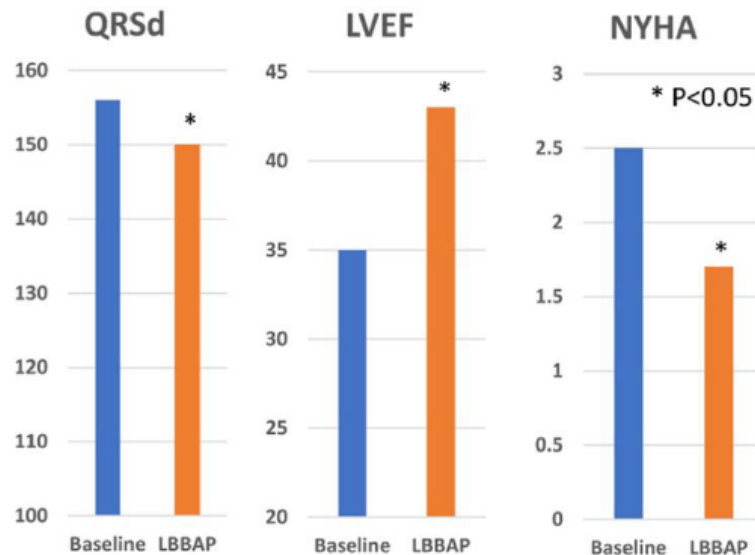
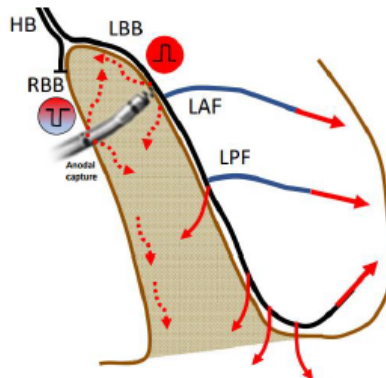
Left bundle branch area pacing in patients with heart failure and right bundle branch block: Results from International LBBAP Collaborative-Study Group

Pugazhendhi Vijayaraman, MD, FHRS, * Oscar Cano, MD,[†]
Shunmuga Sundaram Ponnusamy, MBBS, MD, CEPS-A,[‡] Manuel Molina-Lerma, MD,[§]
Joseph Y.S. Chan, MBBS,^{||} Santosh K. Padala, MBBS,[¶] Parikshit S. Sharma, MD, MPH,^{‡‡}
Zachary I. Whinnett, BMBS, PhD,^{**} Bengt Herweg, MD, FHRS,^{††}
Gaurav A. Upadhyay, MD, FHRS,^{‡‡} Faiz A. Subzposh, MD,^{*} Neil R. Patel, MD, MPH,^{§§}
Dominik A. Beer, DO,^{|||} Agnieszka Bednarek, MD, PhD,^{¶¶} Grzegorz Kielbasa, MD,^{¶¶}
Roderick Tung, MD, FHRS,^{##} Kenneth A. Ellenbogen, MD, FHRS,[†]
Marek Jastrzebski, MD, PhD,^{¶¶}

107/121 (88% di Successo)

KEY FINDINGS

- Left bundle branch area pacing (LBBAP) was feasible in most patients with right bundle branch block (RBBB) requiring cardiac resynchronization therapy (CRT).
- LBBAP was attempted in 121 patients with RBBB eligible for CRT and was successful in 107 patients (88%).
- LBBAP was associated with improvement in clinical and echocardiographic outcomes in patients with RBBB and left ventricular dysfunction.
- Female sex and reduction in QRS duration with LBBAP were predictive of echocardiographic response and super-response.



LBBAP: un'alternativa nei CRT non responder

Upgrading to **LBBP** was found to be feasible and efficacious in terms of achieving significant clinical improvements and echocardiographic remodeling (Chen et al.).

Outcomes of Upgrading to LBBP in CRT Nonresponders

A Prospective, Multicenter, Nonrandomized, Case-Control Study

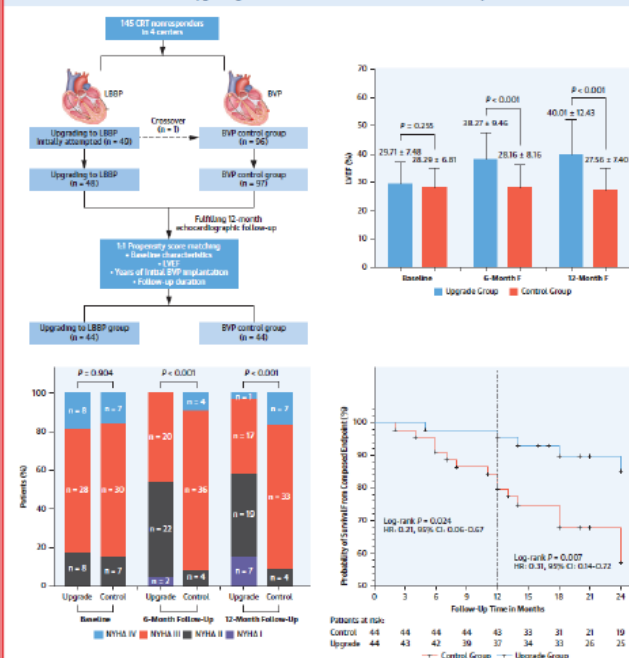
Xueying Chen, MD,^{a,*} Qinchun Jin, MD,^{a,*} Zhaohui Qiu, MD,^b Caizhen Qian, MD,^c Yixiu Liang, MD,^a Jingfeng Wang, MD,^a Shengmei Qin, MD,^a Jin Bai, MD,^a Wei Wang, MD,^a Haiyan Chen, MD,^d Yingxue Dong, MD,^e Weijian Huang, MD,^f Yangang Su, MD^{a,*}

The primary composite endpoint for clinical outcomes in LBBAP group vs Ctrl Group

< HF rehospitalization < mortality < heart transplantation



CENTRAL ILLUSTRATION Upgrading to LBBP is Safe and Efficacious in CRT No-Responders



Chen X, et al. J Am Coll Cardiol EP. 2024;10(7):1018-1030.

BVP = biventricular pacing; CRT = cardiac resynchronization therapy; LBBP = left bundle branch pacing; LVEF = left ventricular ejection fraction.



LOT-CRT: Combinare LBBAP con CRT convenzionale con stimolazione da seno coronarico (LOT-CRT) determina migliore resincronizzazione elettrica e meccanica nei pazienti con NIVCD

Electrical Resynchronization and Clinical Outcomes During Long-Term Follow-Up in Intraventricular Conduction Delay Patients Applied Left Bundle Branch Pacing-Optimized Cardiac Resynchronization Therapy
Xueying Chen, et al. *Circ Arrhythm Electrophysiol.* 2023;16:e011761. DOI: 10.1161/CIRCEP.122.011761

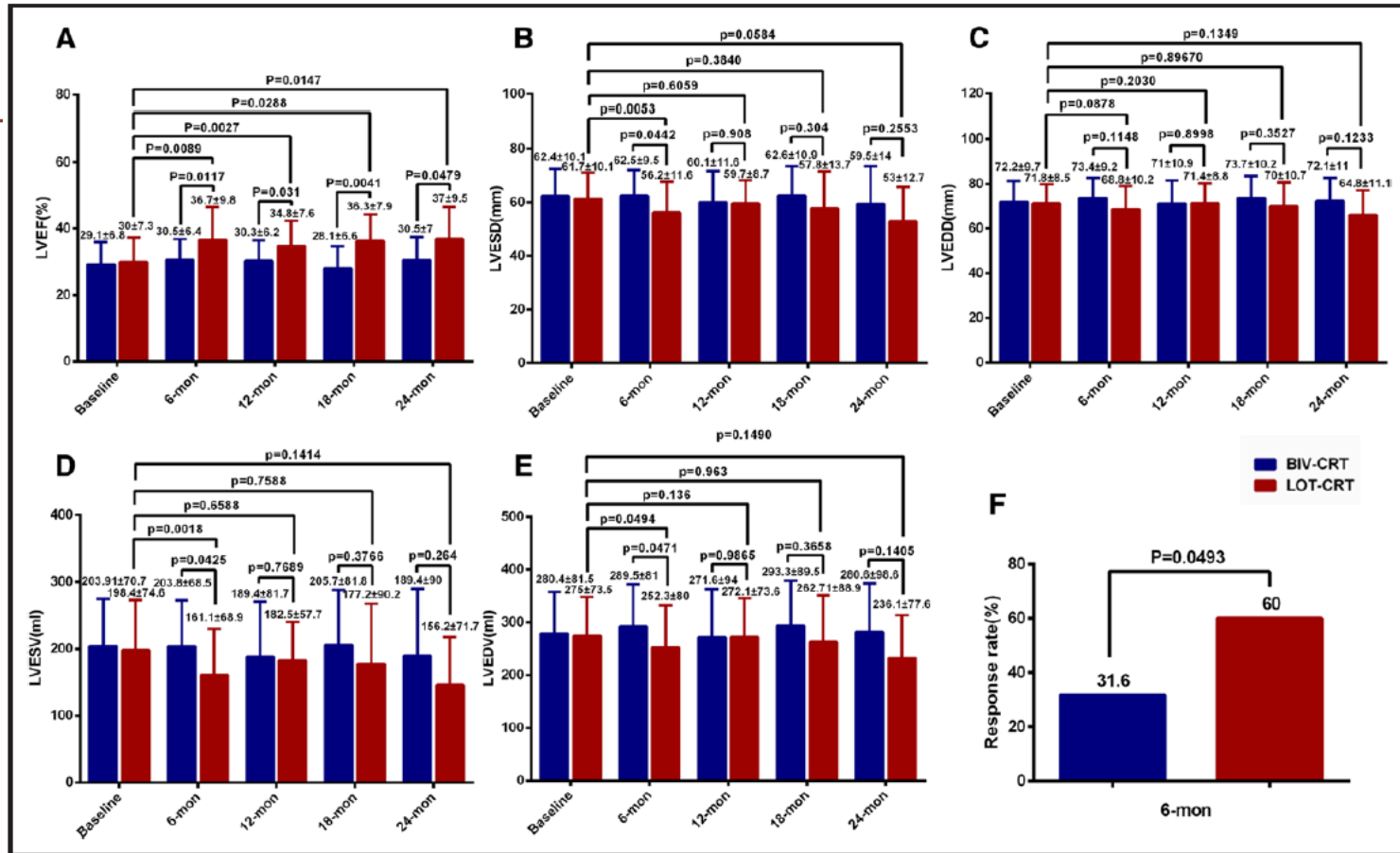


Figure 4. Echocardiographic response after biventricular and left bundle branch pacing-optimized cardiac resynchronization therapy.

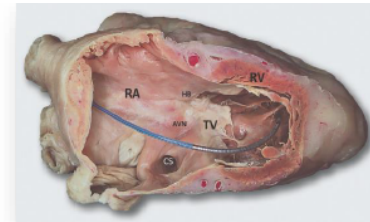
A, left ventricular ejection fraction (LVEF). **B**, left ventricular end-systolic diameter (LVESD). **C**, left ventricular end-diastolic diameter (LVEDD). **D**, left ventricular end-systolic volume (LVESV). **E**, left ventricular end-diastolic volume (LVEDV). **F**, Response rate.

Prospective future: LBBAD

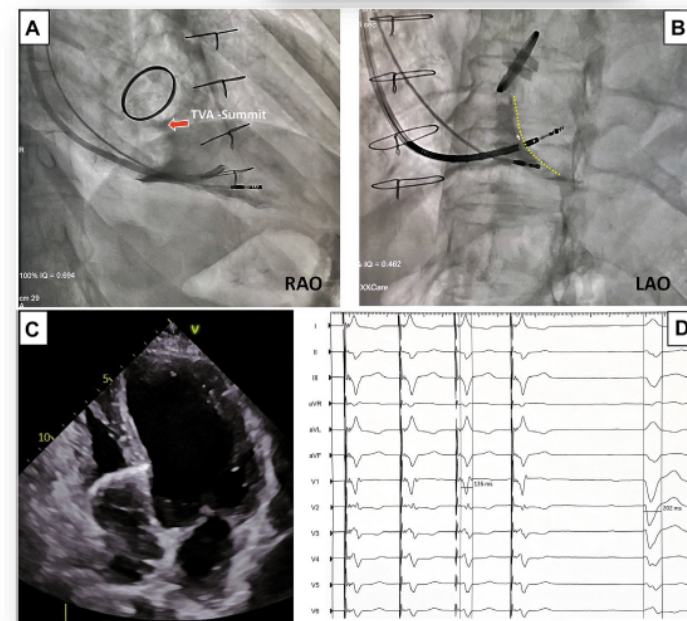
Standard Defibrillator Leads for Left Bundle Branch Area Pacing

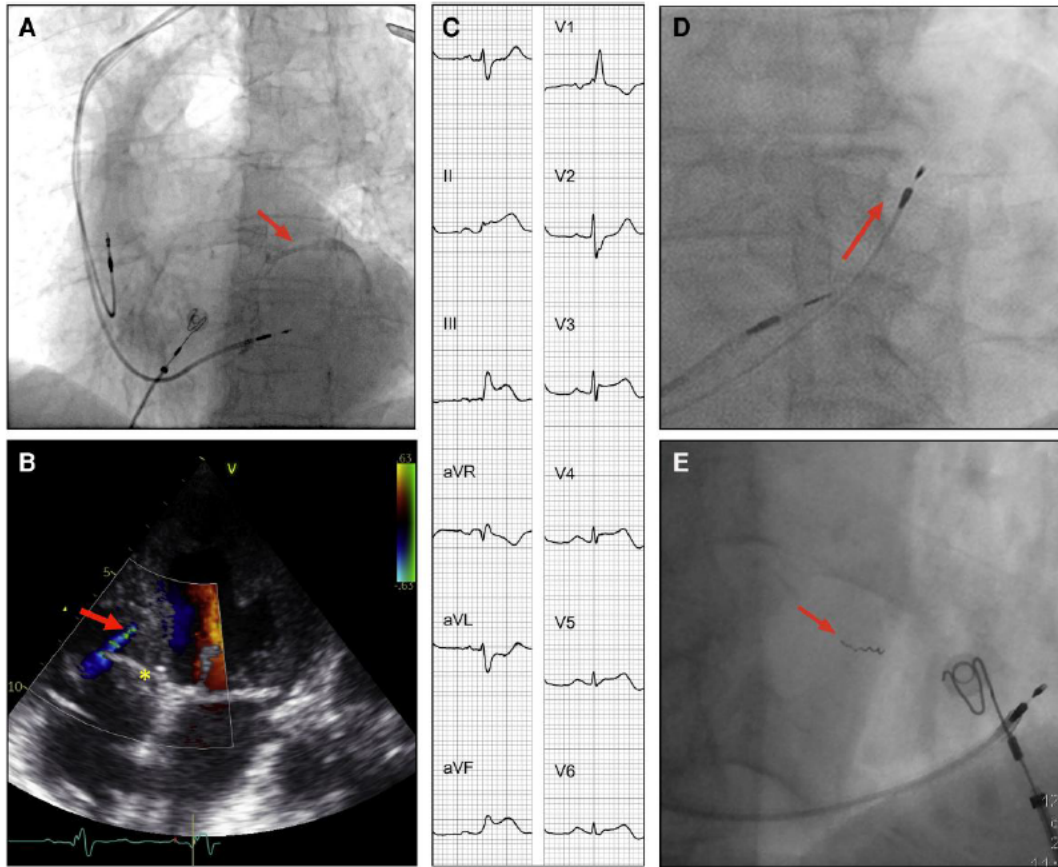
First-in-Man Experience and Short-Term Follow-Up

Guram Imnadze, MD,^a Thomas Fink, MD,^a Thomas Eitz, MD,^b Yuri Bocchini, MD,^a Lilil Antonyan, MD,^a
Karen Harutyunyan, MD,^a Valérian Valiton, MD,^c Maxim Didenko, MD,^a Philipp Sommer, MD,^a Haran Burri, MD^c



Parameter	@ implant	@ day 1	@ last follow-up (5.1±1.1 months)
Capture threshold (V/0.5ms)	0.8±0.2*	0.5±0.1	0.7±0.1
Pacing impedance (Ω)	527±8*	449±67	421±73
Sensing threshold (mV)	8.7±3.4	7.7±3.3	8.9±3.1
Paced QRS duration (ms)	124±15*	133±12	135±15
V6 R-wave peak time (ms)	88±20*	83±20	80±16ms
V6V1 interpeak interval (ms)	39±4*	43±10 [#]	41±9 [#]





Complications of LBBAP

- (A) Coronary venous fistula (arrow points to contrast in great cardiac vein).
- (B) Coronary artery fistula (arrow points to the blood jet near the lead entry site).
- (C) Acute ST-segment elevation in leads II, III, aVF and V3-V6 with concomitant chest pain during left bundle branch area pacing lead deployment.
- (D) Late lead perforation into left ventricular cavity
- (E) Helix entrapment with subsequent lead break during attempts to unscrew/remove



Caso clinico Nocera Inferiore: CSP-CRTD

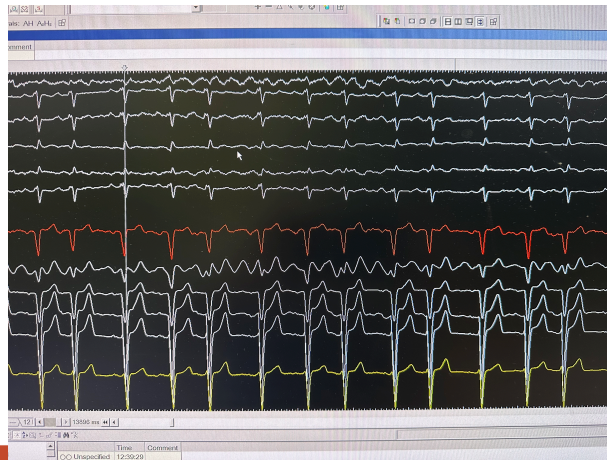
NIVCD – FE 35%

QRS da 144 ms a 95 ms

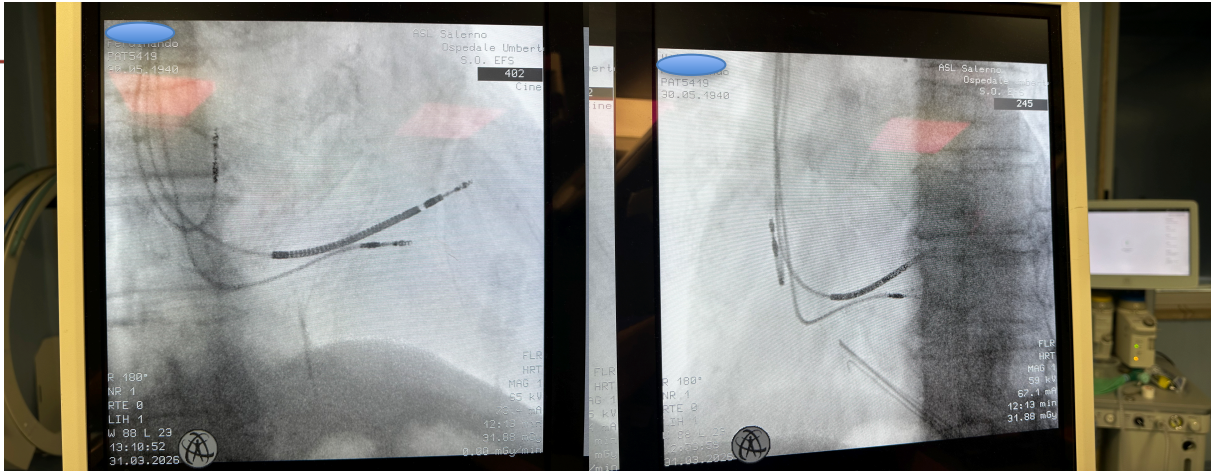
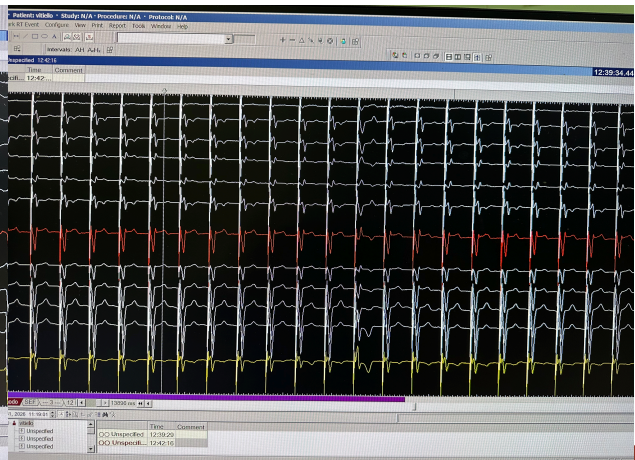
Upgrade FE 35% -> 42%

GLS -12% -> -16%

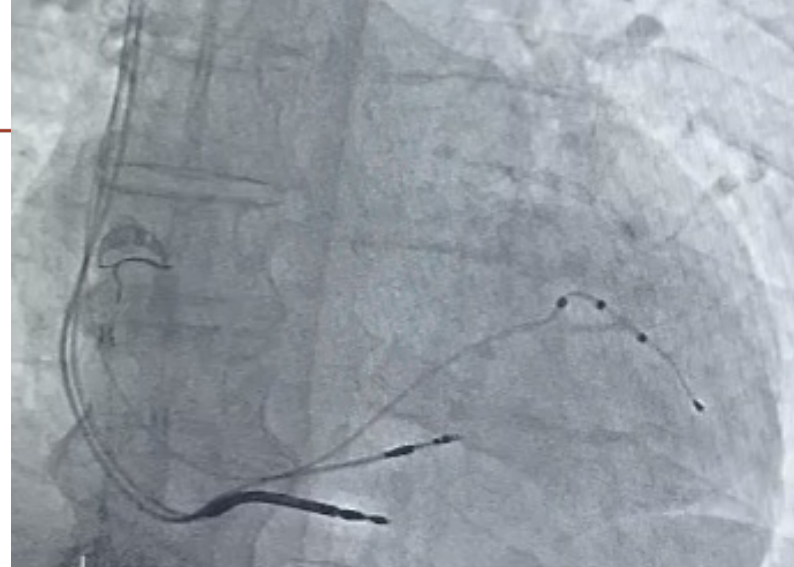
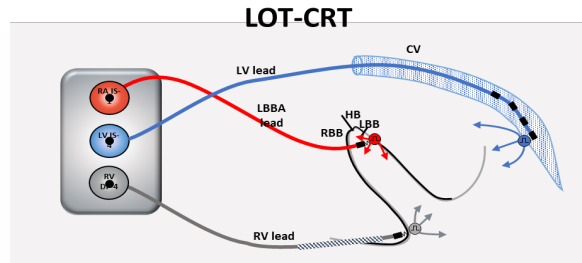
Baseline



CSP-CRT



Caso clinico LOT-CRT Nocera Inferiore



QRS= 144ms

QRS= 128 ms

QRS=102ms

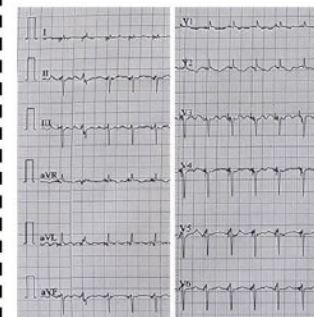
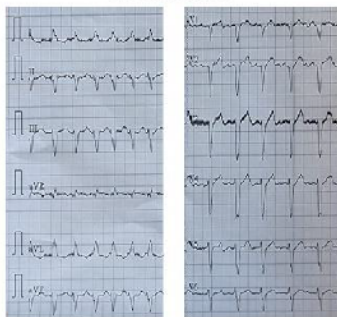
QRS=82ms

SPONTANEO

BIV-CRT

LBBAP

LOT-CRT



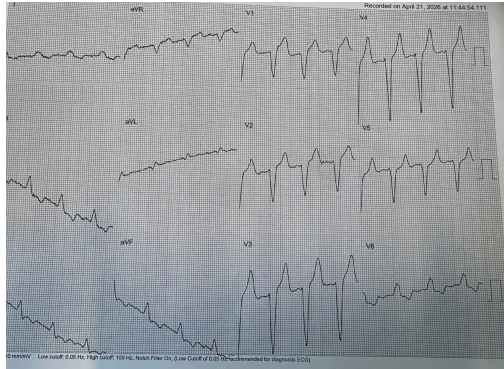
Programmazione:
Rit. LBBAP-BIV= 25 ms
VV = Simultaneo



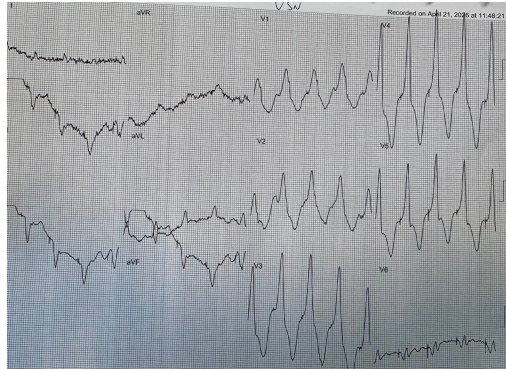
Caso clinico Nocera Inferiore

CRT non responder → upgrade LOT-CRT

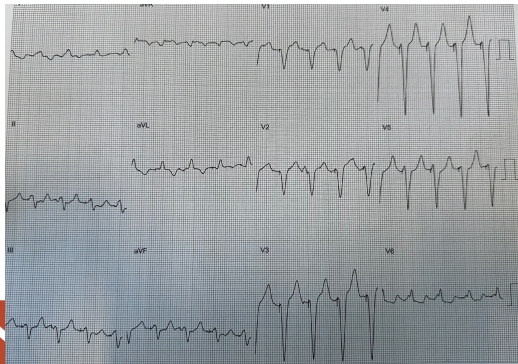
Basale



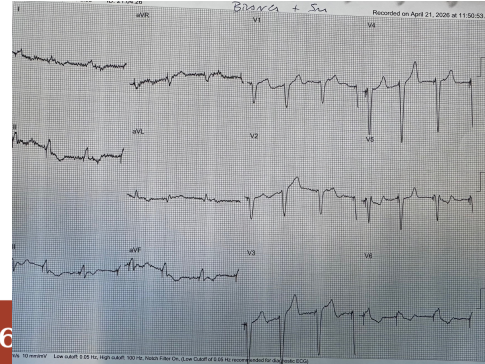
Biv-CRT



LBBAP

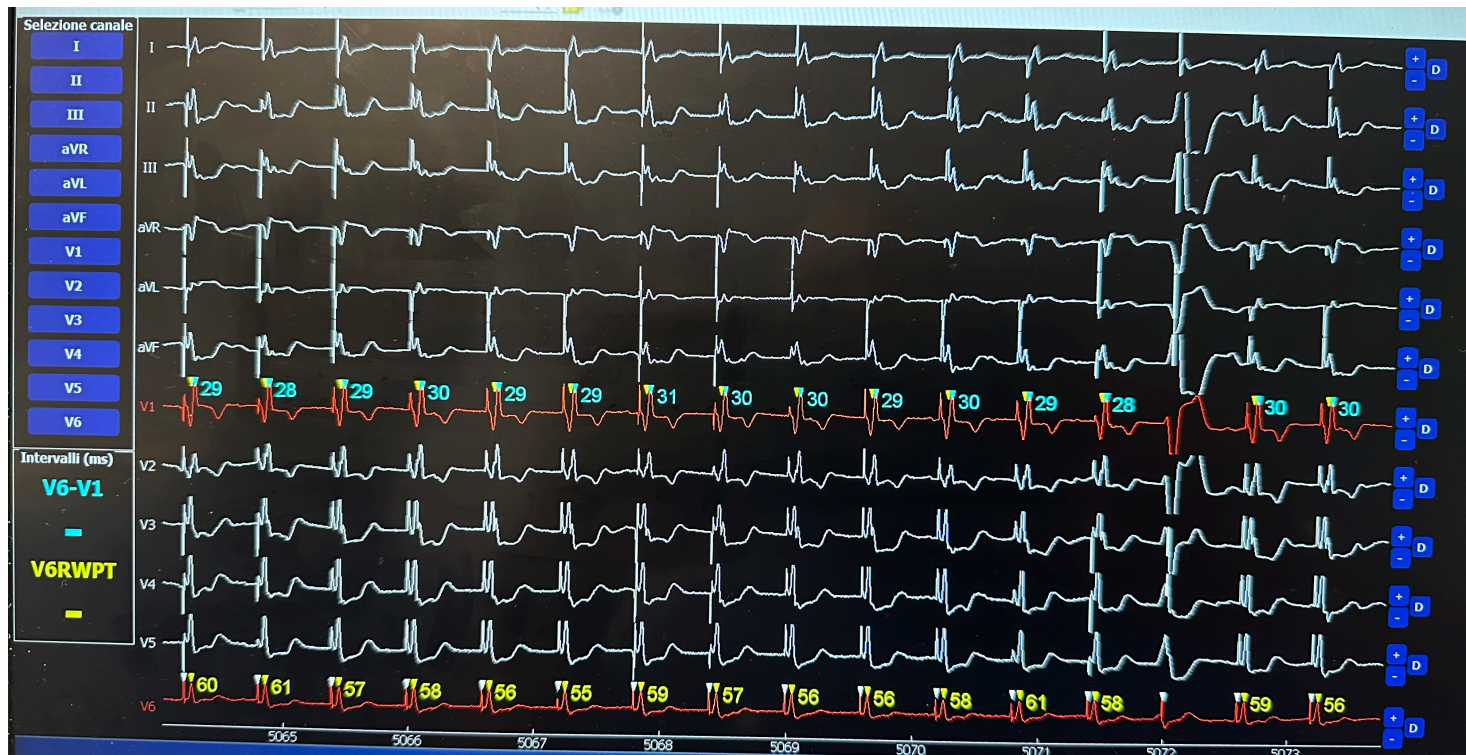


LOT-CRT



LBBOT: left branch BOT

Sistema di monitoraggio battito-battino – LVAT e interpicco V6-V1



Conclusions

Small number of patients with NIVCD implanted with LBBAP

Necessity of randomized trial to assess benefits of CSP-CRT compared with BiV-CRT

Encouraging results in patients with NIVCD implanted with LOT-CRT



