Gravidita a laktace
u
hereditárních arytmických syndromů

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INTERNÍ KARDIOLOGICKÁ KLINIKA FN BRNO a LF MU

MUNI MED

Hereditární arytmické syndromy

Arytmie + synkopy + náhlá smrt + familiární výskyt

- syndrom dlouhého QT intervalu (LQTS) 1:2500
- katecholaminergní polymorfní komorová tachykardie (CPVT) (1:10.000)
- Brugada syndrom (1:???)
- syndrom krátkého QT intervalu (1:???)

Hereditární arytmické syndromy

Spouštěčem arytmií jsou typicky situace spojené s náhlým zvýšením tonu sympatiku a vyplavením katecholaminů

- fyzická zátěž
- emoční stres
- Bolest

- léky s proarytmickým potenciálem

Historie

2007

Journal of the American College of Cardiology
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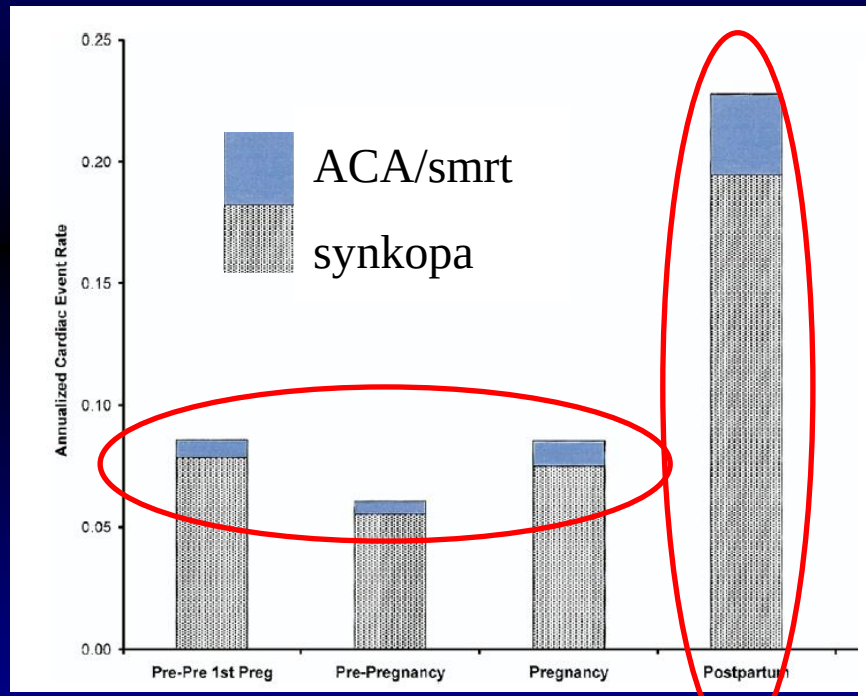
Vol. 49, No. 10, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2006.09.054

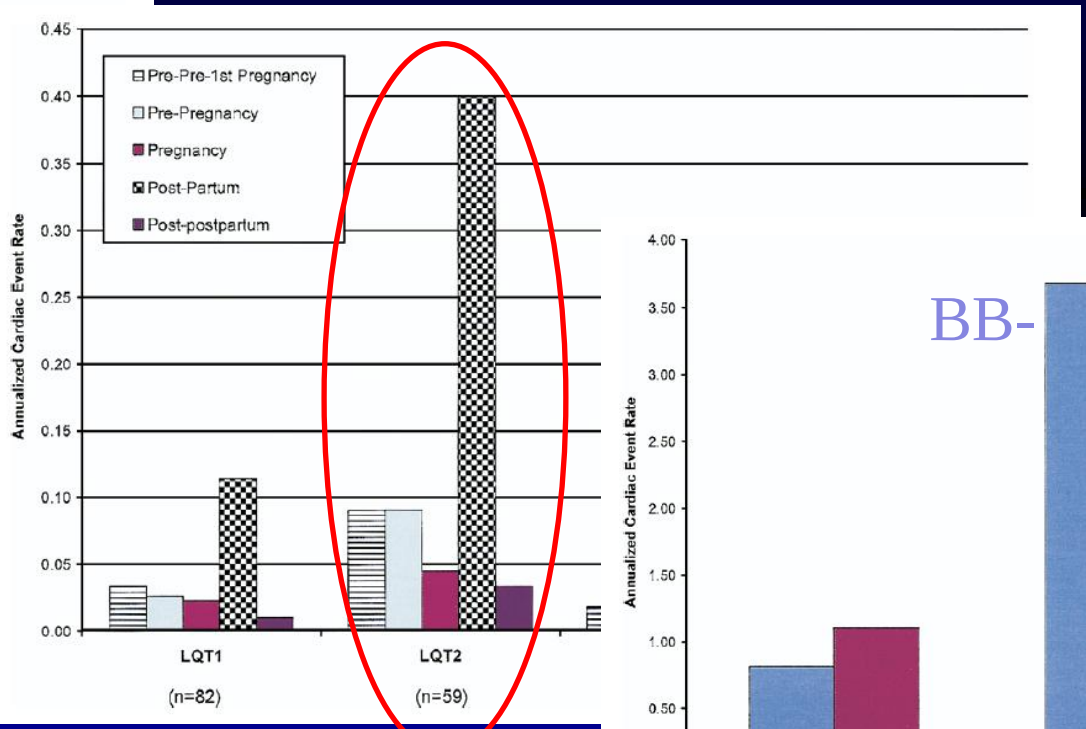
Heart Rhythm Disorders

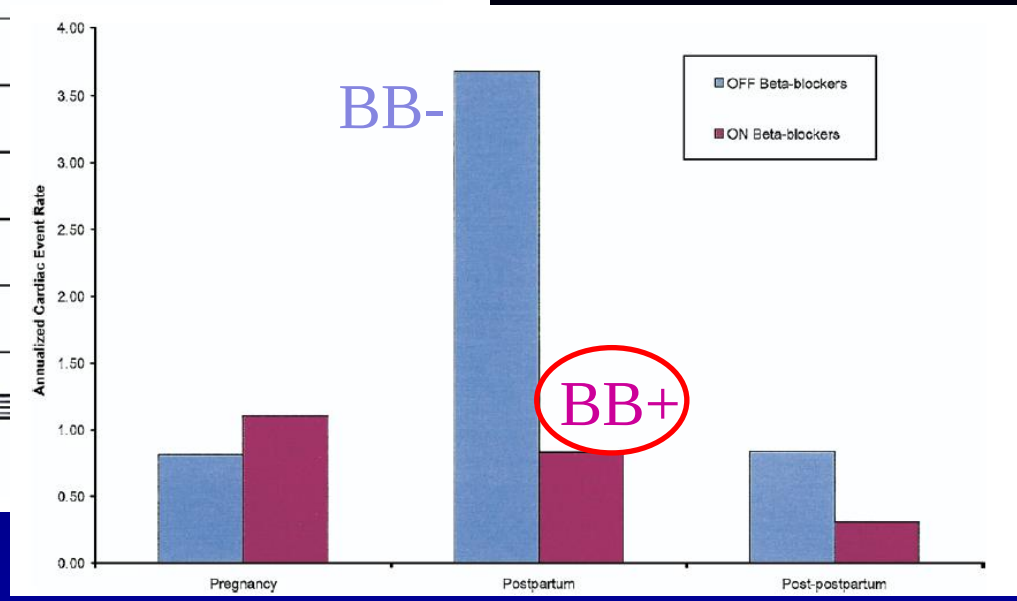
Long QT Syndrome and Pregnancy

Rahul Seth, MD,* Arthur J. Moss, MD,* Scott McNitt, MS,* Wojciech Zareba, MD, PHD,*

Retrospektivní analýza průběhu těhotenství a postpartálního období u 391 prvorodiček z mezinárodního LQT registru







9 měsíců po porodu
2,7x vyšší riziko synkopy
4,1x vyšší riziko život ohrožující příhody

Revista Española de Cardiología (English Edition)
Volume 67, Issue 3, March 2014, Pages 176-180

Original article

The Clinical Significance of Pregnancy in Brugada Syndrome

Trascendencia clínica del embarazo en el síndrome de Brugada

Moisés Rodríguez-Mañero, Rubén Casado-Arroyo, Andrea Sarkozy, Eva Leysen, Juan Antonio Sieira, Mehdi Namdar, Gulio Conte, Moisés Levinstein, Gian-Battista Chierchia, Carlo de Asmundis, Pedro Brugada

- 219 těhotenství u 104 pacientek s BrS
- v průběhu těhotenství a peripartálního období 6x synkopa, žádné úmrtí, žádné výboje z ICD
- těhotenství nevedlo k nárůstu příhod

JACC: CLINICAL ELECTROPHYSIOLOGY VOL. 5, NO. 3, 2019

PUBLISHED BY ELSEVIER

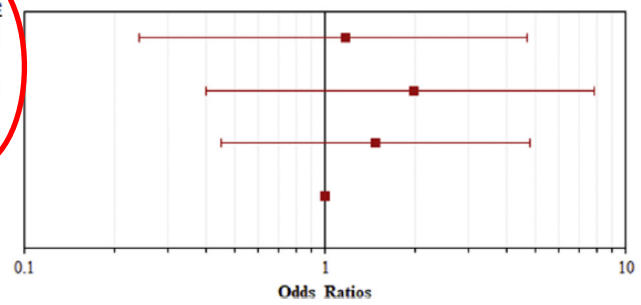
Pregnancy in Catecholaminergic Polymorphic Ventricular Tachycardia

Christopher C. Cheung, MD,[a,*] Krystien V. Lieve, MD,[b,*] Thomas M. Roston, MD,[a] Martijn H. van der Ree, MD,[b] Marc W. Deyell, MD,[a] Jason G. Andrade, MD,[a] Zachary W. Laksman, MD,[a] Eline A. Nannenberg, MD, PhD,[b,c] Rafik Tadros, MD, PhD,[b] Benjamin Pang, PhD,[d] Julie Rutberg, MS,[d] Martin S. Green, MD,[d] Susan Conacher, MSc,[e] Colette M. Seifer, MD,[f] Jason D. Roberts, MD, MAS,[f] Christian Steinberg, MD,[g] Shubhayan Sanatani, MD,[h] Arthur A. Wilde, MD,[b] Andrew D. Krahn, MD[a]

- 228 těhotenství u 96 pacientek s CPVT (drtivá většina před stanovením dg)

FIGURE 2 Forest Plot of Event Rate Ratios

	Rate Ratio	95% CI	p-value
Pregnancy	1.17	0.24-4.71	0.802
Postpartum	1.96	0.40-7.85	0.362
Peripartum	1.47	0.45-4.81	0.518
Non-Pregnant	1.00	Reference	n/a



- těhotenství nevedlo k nárůstu příhod
- žádná ze symptomatických pacientek nebrala betablokátor

ESC European Society of Cardiology
European Heart Journal (2018) 39, 3165–3241
doi:10.1093/eurheartj/ehy340
ESC GUIDELINES

2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy

Celkem 7 řádků…

tively high rate (50%) of spontaneous recovery after delivery. Non-selective beta-blockers should be continued throughout pregnancy and during the post-partum period (at least 40 weeks after delivery)[323] in patients with congenital LQTS[332] and those with catecholaminergic polymorphic VT.[72,333] Exceptions may be LQTS patients without prior syncope or torsade de pointes (TdP), or any other risk profile, for whom a selective beta-blocker may be chosen.

Jedno „velmi užitečné“ doporučení……

Beta-blocking agents are recommended during pregnancy and post-partum in patients with long QT syndrome or catecholaminergic polymorphic VT.[72,323]	I	C

Jedna tabulka stratifikace rizika, která ale nespecifikuje, co je „low“, „moderate“, „high“ risk…

Table 6 Recommended surveillance levels at time of delivery in women with arrhythmias

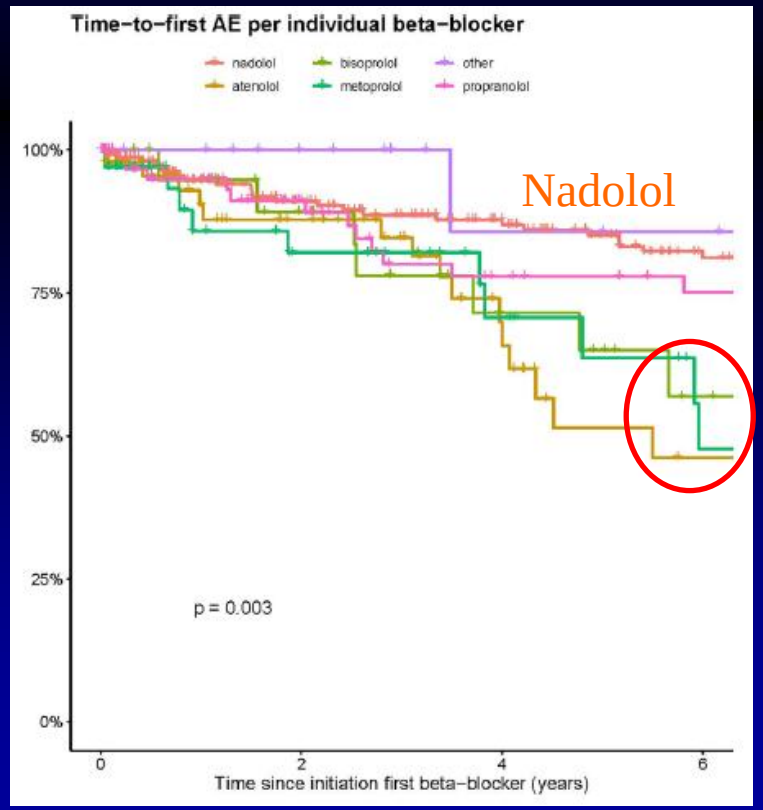
Risk for arrhythmia with haemodynamic compromise at delivery		Level of surveillance[a]	Class[b]	Level[c]
Low-risk	PSVT, AF, idiopathic VT, low-risk LQTS, WPW syndrome	1	I	C
Medium-risk	Unstable SVT, VT, those with an implanted ICD, VT and structural heart disease, Brugada syndrome, moderate risk: LQTS, catecholaminergic polymorphic VT	2	I	C
High-risk for life threatening arrhythmia	Unstable VT in structural heart disease/congenital heart disease, unstable VT/TdP in high-risk LQTS patients, short QT syndrome, high-risk catecholaminergic polymorphic VT	3	I	C

Betablokátory – které a kdy?

Ahn, et al, Plos One 2017
- metanalýza zahrnující 9727 LQT pacientů z 10 studií
- u LQT1 fungují atenolol, propranolol, nadolol
- u LQT2 je účinný jen nadolol
- metoprolol nesnižuje riziko u žádného genotypu

Leren IS, et al. Heart Rhythm 2016
- 34 pacientů s CPVT
- Nadolol snížil četnost i komplexitu komorových arytmií
- při β1 selektivních BB arytmie stejné jako bez léčby

Peltenburg PJ, et al. Circulation 2022
- 329 dětských pacientů s CPVT
- při β1 selektivních BB bylo HR 2-3x vyšší oproti nadololu



Nadolol

Bisoprolol
Metoprolol
Atenolol

2020

CONTEMPORARY REVIEW Heart Rhythm, Vol 17, No 2, February 2020

Caring for the pregnant woman with an inherited arrhythmia syndrome

Thomas M. Roston, MD,*† Christian van der Werf, MD, PhD,‡
Christopher C. Cheung, MD,* Jasmine Grewal, MD,* Brianna Davies, MSc,*
Arthur A.M. Wilde, MD, PhD, FHRS,‡ Andrew D. Krahn, MD, FHRS*

Bezpečnost farmakoterapie v těhotenství

Safety of Common Anti-Arrhythmic Drugs for Inherited Arrhythmia in Pregnancy

	Propranolol	Metoprolol[1]	Nadolol[2,3]	Atenolol	Mexiletine[2]	Flecainide[2]	Quinidine[2]	Sotalol[4]	Amiodarone
1st Trimester	✓	✓	?	✗	?	?	?	✓	✗
2nd Trimester	✓	✓	?	✗	?	✓	?	✓	✗
3rd Trimester	✓	✓	?	✗	?	✓	?	✓	✗
Breastfeeding & Post-partum	✓	✓	✗	✗	?	✓	✗	✓	✗

1. Metoprolol is not advised for LQT2 in the post-partum period or in high risk patients
2. For drugs with limited fetal safety data, suggest shared-decision making approach based on individual risk profile
3. Nadolol should be considered for CPVT, suggest shared-decision making approach based on individual risk profile
4. Sotalol (Category B) is a reasonable alternative to amiodarone in ACM

the maximum and/or highest tolerated dose, is essential, especially for LQT2. Propranolol is a good option in this setting as it can be taken while breastfeeding, whereas nadolol is generally not recommended but often continued when

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Riziková stratifikace

Risk for Arrhythmia with Hemodynamic Compromise at Labor & Delivery	Inherited Arrhythmia Syndrome Phenotype	Level of Surveillance
Low-risk	• BrS with no previous events • LQTS with no previous events and QTc ≤470 • Gene-positive CPVT without any phenotype	1
Medium-risk	• BrS and LQTS with remote events • LQTS with no previous events and QTc >470 • CPVT with no recent events and only isolated PVCs on recent EST • ACM with no recent events or NSVT • IVF, SQTS & ERS with no recent events	2
High-risk	• CPVT with recent events and/or recent EST with bigeminal PVCs or higher grade arrhythmia • ACM with recent events and/or NSVT • Any other inherited arrhythmia syndrome with recent events	3

Actions to be Planned for Onset of Labor and Delivery	Surveillance		
	1	2	3
Involvement of a Pregnancy Heart Team with expertise in inherited arrhythmia syndromes	X	X	X
Awareness of contra-indicated drugs in the setting of select channelopathies	X	X	X
Continuous telemetry monitoring			X
Intravenous Line		X	X
Preparation of intravenous beta-blocker or anti-arrhythmic drug on unit		X	X
External cardioverter defibrillator on unit		X	X
Arterial line			X

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1st Trimester	✓	✓	?	✗	?	?	?	✓	✗
2nd Trimester	✓	✓	?	✗	?	✓	?	✓	✗
3rd Trimester	✓	✓	?	✗	?	✓	?	✓	✗
Breastfeeding & Post-partum	✓	✓[1]	✗	✗	?	✓	✗	✓	✗

	Therapy for Acute Presentation	Transition to Chronic Therapy
Long QT	1st line: IV/PO beta-blocker 2nd line: IV $MgSO_4$, lidocaine, mexiletine 3rd line: Transvenous pacing*	Increase beta-blocker ± add mexiletine Consider K^+ supplement ± LCSD (best delayed until post-partum) Assess for ICD indication*
Catecholaminergic Polymorphic VT	1st line: IV/PO beta-blocker 2nd line: IV/PO flecainide 3rd line: Temporary sympathetic block	Increase beta-blocker ± flecainide Consider LCSD (best delayed until post-partum)
Brugada	1st line: IV isoproterenol 2nd line: PO quinidine	Add quinidine, ± possibly sotalol if SQTS Assess for ICD indication*

ESC European Society of Cardiology
European Heart Journal (2025) **00**, 1–107
https://doi.org/10.1093/eurheartj/ehaf193

ESC GUIDELINES

2025 ESC Guidelines for the management of cardiovascular disease and pregnancy

Developed by the task force on the management of cardiovascular disease and pregnancy of the European Society of Cardiology (ESC)

Endorsed by the European Society of Gynecology (ESG)

Nová doporučení se již problematice arytmických syndromů podrobně věnují.
Významnou roli hraje „Pregnancy Heart Team“.

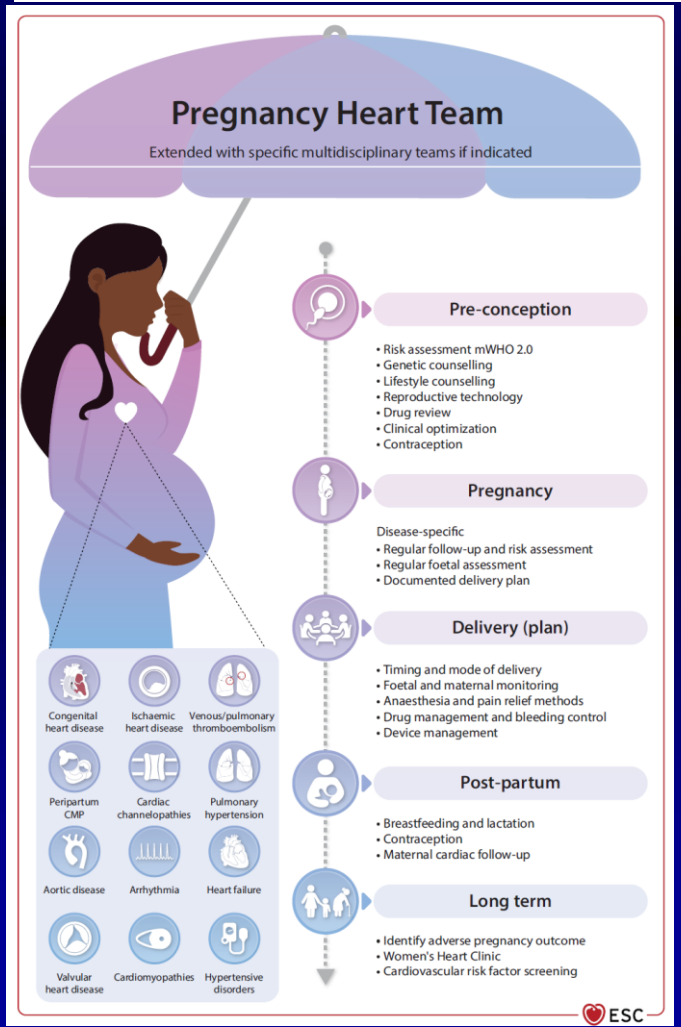

Table 6 Modified World Health Organization 2.0 classification of maternal cardiovascular risk

mWHO 2.0 I	mWHO 2.0 II	mWHO 2.0 II–III	mWHO 2.0 III	mWHO 2.0 IV
Arrhythmias				
Atrial or ventricular ectopic beats, isolated.	Most supraventricular arrhythmias. Bradycardia requiring pacemaker.	Low-risk LQTS: no previous events + on full dose beta-blocker therapy. Low-risk CPVT: well controlled by medical therapy. BrS with no previous events.	Sustained ventricular tachycardia from any aetiology. LQT2 (post-partum). Symptomatic CPVT and LQTS not adequately controlled by therapy. BrS with previous events.	
Obstetric and cardiac care during pregnancy		Shared care with local hospital + Pregnancy Heart Team	Care led by Pregnancy Heart Team	
Location of delivery		Shared care with local hospital + Pregnancy Heart Team. Location depends on CV status and evolution of pregnancy	Expert centre, care led by Pregnancy Heart Team	

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Monitoring and treatment of hypokalaemia and hypomagnesaemia is recommended in pregnant women with primary arrhythmia syndromes suffering from hyperemesis.[334]	I	C

Všechna antiemetika prodlužují QT interval!!!

Long QT syndrome		
Beta-blockers[c], with pre-pregnancy dose and with nadolol and propranolol as drugs of choice, are recommended during pregnancy in women with LQTS.[312–316,335]	I	B
It is recommended to continue beta-blocker therapy during lactation in women with LQTS to reduce arrhythmic risk.[148,336]	I	B
Pre-pregnancy beta-blocker dose of nadolol or propranolol, is recommended in women with LQT2, particularly in the post-partum period, which represents a high-risk period for life-threatening arrhythmias.[148,313,315]	I	B

- dosud neléčené pacientky s LQTS by měly v těhotenství léčbu zahájit – kvůli zvýšenému riziku po porodu
- v průběhu laktace je preferovaným lékem propranolol (prakticky neproniká do mléka, relativní dávka nadololu pro kojence je 4-7 %)
- u pacientek s vysokým rizikem zvážit pokračující nadolol, změna medikace po porodu je riziková
- zhodnocení EKG u novorozence po porodu a po 2 týdnech

Brugada syndrome		
Quinidine therapy should be considered in pregnant women with BrS who have arrhythmic events during pregnancy.[337,338]	IIa	C

Catecholaminergic polymorphic ventricular tachycardia		
Beta-blockers[c], with pre-pregnancy dose and with nadolol and propranolol as drugs of choice, are recommended during pregnancy and lactation in women with CPVT.[43,148,252]	I	C
Flecainide, in addition to beta-blockers, is recommended in women with CPVT who experience cardiac events such as syncope, VT, or cardiac arrest during pregnancy.	I	C
It is recommended that women with CPVT who are stable on beta-blockers (nadolol or propranolol as drugs of choice) and flecainide before pregnancy continue both drugs during pregnancy and post-partum.	I	C
The use of beta-blockers[c] during pregnancy and lactation should be considered in phenotype-negative women with a CPVT P/LP variant.[148]	IIa	C

Specifická doporučení k porodu

- nízkorizikové pacientky mohou rodit v lokálních nemocnicích (Pregnancy heart team na telefonu)
- u pacientek s anamnézou arytmických příhod by porod měl probíhat v expertním centru s adekvátní monitorací (ionty, EKG?)
- způsob vedení porodu podle porodnických indikací
- adekvátní analgézie k omezení adrenergní aktivace
- ev. kontrola tepové frekvence do 110/min u CPVT pacientek i. v. BB
- pozor na proarytmický potenciál analgetik/anestetik!
  propofol a blokátory Na kanálu jsou kontraindikovány u BrS

www.crediblemeds.org www.brugadadrugs.org

Závěrem

- Pregnancy heart team
- Nová doporučení významně rozvolňují tradiční kontraindikace farmakoterapie v graviditě a laktaci
- Propranolol je bezpečný a nadolol se nevysazuje
- shared decision
- U většiny pacientek s arytmickými syndromy nejsou peripartální rizika vysoká
- nezapomínat na proarytmický potenciál jakékoli medikace

www.crediblemeds.org www.brugadadrugs.org

Kardiogenetická ambulance IKK FN Brno

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Prof. MUDr. Tomáš Novotný, Ph.D.

Doc. MUDr. Irena Andršová, Ph.D.

MUDr. Kateřina Helánová, Ph.D.

- Komplexní diagnostika včetně genetického vyšetření ve spolupráci s Ústavem lékařské genetiky a genomiky FN Brno od roku 2000 (první genotypizovaná LQT rodina v ČR)
- Kaskádový screening v rodinách zemřelých náhlou srdeční smrtí (+ spolupráce s Ústavem soudního lékařství FN UsA a LF MU, Brno