

Insuffisance cardiaque chez les femmes. Est-ce qu'une prise en charge particulière est nécessaire?



**Dr N Hrynychshyn
CNCH PARIS 2018**



Collège
National des
Cardiologues des
Hôpitaux

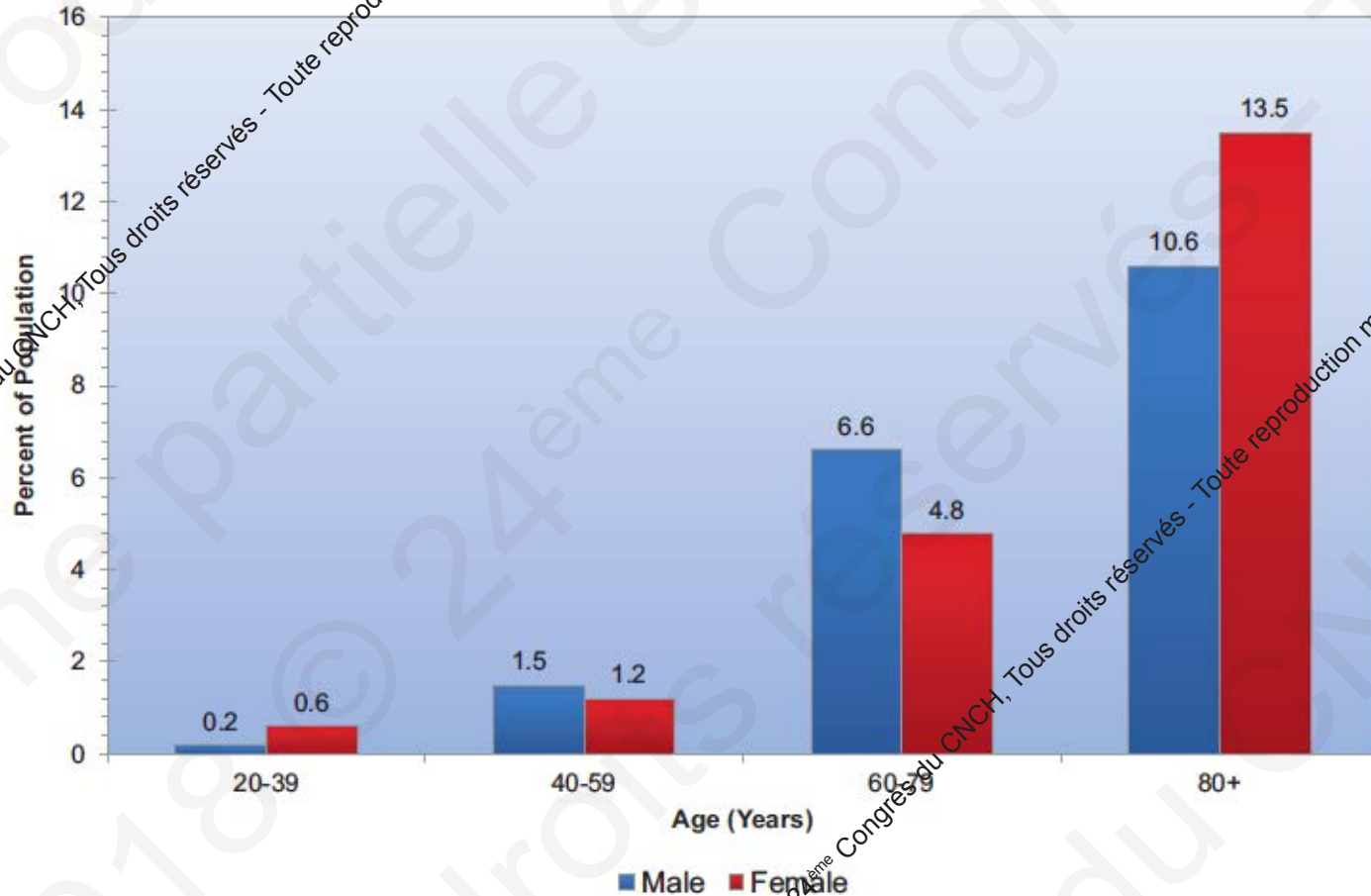
DÉCLARATION DE RELATIONS PROFESSIONNELLES

Conférencier : Hrynychshyn Nataliya, Pontoise

Je n'ai pas de lien d'intérêt potentiel à déclarer

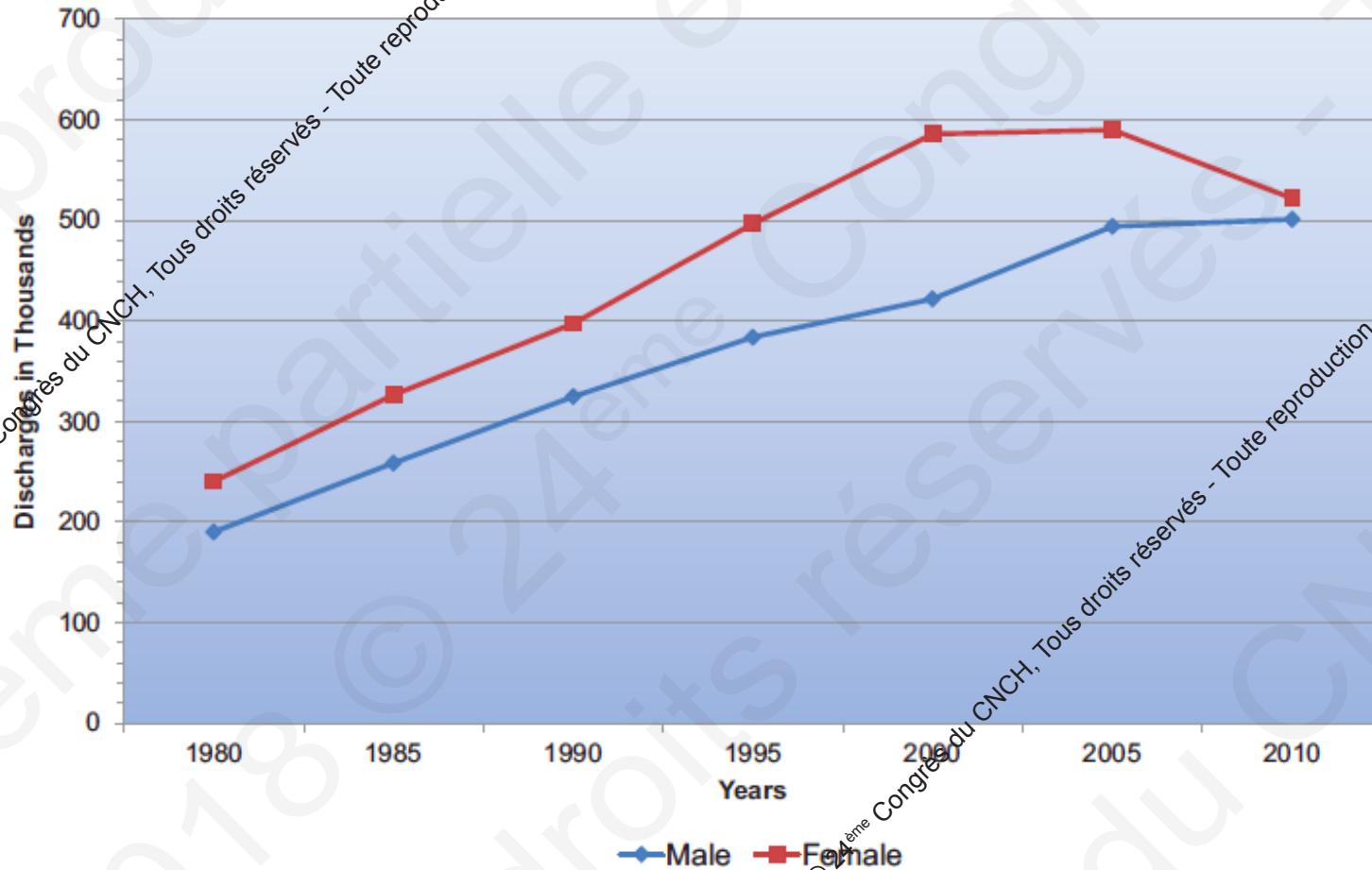
Prévalence d'insuffisance cardiaque par l'âge et sexe

National Health and Examination survey 2009-2012



Hospitalisation pour l'insuffisance cardiaque en fonction de sexe

Etats-Unis 1980-2010



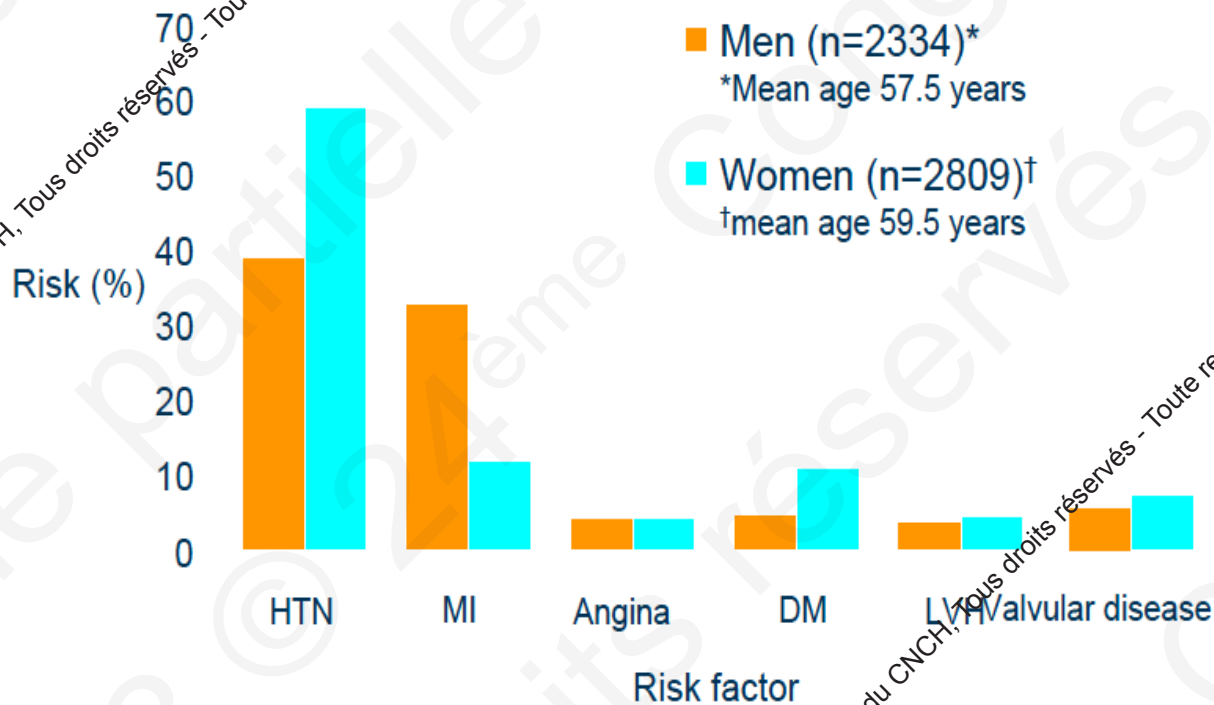
Tendances de mortalité cardiovasculaire en fonction de sexe

Etats-Unis 1979-2013



MORTALITE CV
PLUS HAUTE
CHEZ LES FEMMES

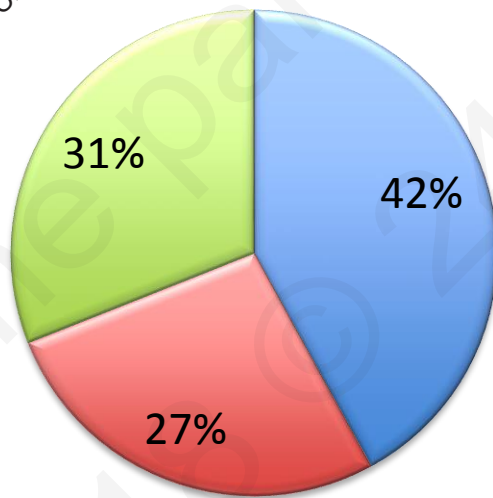
Framingham Study: 20-year follow-up



FE VG en fonction de sexe

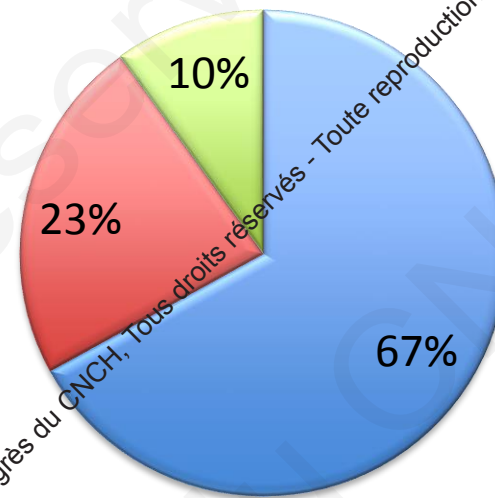
Hommes

- Normale FE VG > 55%
- Modérée FE VG 45-54%
- Moyenne/Sévère <45%



Femmes

- Normale FE VG >55%
- Modérée FE VG 45-54%
- Moyenne/Sévère FE VG <45%



Kizman D et al. J Am Cardiol 2001; 87/ 413-419

:

Comorbidités chez les femmes

	All Patients (n=857)	Women (n=236)	Men (n=621)	P-Value
Age (years, mean (SD))	67 (13)	70 (13)	66 (12)	<0.01
<i>Predominant heart failure etiology (n, %)</i>				
Coronary artery disease	425 (49.9)	101 (42.8)	328 (52.8)	0.01
Others	427 (50.1)	135 (57.2)	293 (47.2)	
<i>Comorbidities (n, %)*</i>	592 (69.1)	176 (74.6)	416 (67)	0.03
<i>History of depression (n, %)</i>	92 (10.7)	45 (19.1)	47 (7.6)	<0.01
<i>Heart Failure characteristics</i>				
NYHA functional class				
III-IV (n, %)	362 (42.2)	126 (53.4)	236 (38.0)	0.02
LVEF, %, mean (SD)	30 (8.2)	30 (8.1)	31 (7.7)	0.07
NTproBNP, pg/ml, median (IQR)	2794.0 (1031.5-6573.0)	3639.0 (1377.0-8173.0)	2561.0 (30.8-6235.5)	<0.01
<i>Psychometric assessment</i>				
N=846: KCCQ OSS, median (IQR)	56.7 (38.9-75.0)	47.9 (29.8-65.2)	59.4 (41.9-78.1)	<0.01
N=846: KCCQ CSS, median (IQR)	61.5 (42.6-79.7)	54.2 (32.1-70.1)	65.1 (46.3-83.3)	<0.01
PHQ-9 sum- score, median (IQR)	6.0 (3.0-11.0)	7.5 (4.0-13.0)	6.0 (3.0-11.0)	0.02
PHQ-9 ≥10 (n, %)	286 (33.4)	92 (39.0)	194 (31.2)	0.03

Particularités pharmacocinétiques chez les femmes

TABLE 1 Variations in PK properties of drugs in women

PK Property	Effect in Women	Cause
Absorption	Less oral drug absorption	Less gastric acid secretion Slower GI motility and transit time
Distribution	Larger for lipophilic drugs Smaller for hydrophilic drugs	Greater body fat Lower total body water
Metabolism	Phase I Increased activity of CYP2B6, CYP2D6, CYP3A4 Decreased activity of CYP1A2, CYP2E1 Phase II Increased activity of xanthine-oxidases Decreased activity of N-acetyltransferases, sulfotransferases, methyltransferases	Variations in enzyme activity due to pregnancy, menopause, OC use and menstruation
Excretion	Lower but marginal difference when normalized for body weight	Decreased renal blood flow, GFR, and tubular secretion and reabsorption

Femmes: moins incluses dans les études cliniques?

TABLE 2. Participation of Women in Clinical Trials on Heart Failure With Depressed Ejection Fraction

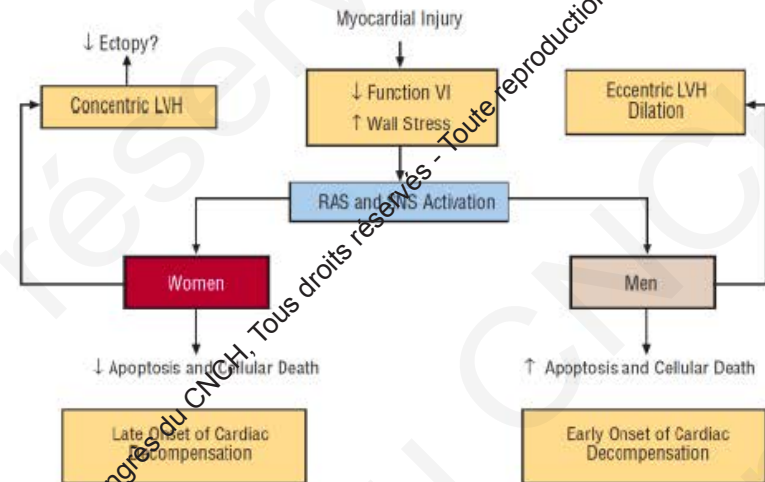
Study	No. of Patients	No. of Women	Women, %
CONSENSUS-I ³⁷	253	75	30
SOLVD-T ³⁸	2569	504	23
SOLVD-P ³⁹	4228	476	31
ELITE-I ⁴⁰	722	240	31
ELITE-II ⁴¹	3152	966	30
MERIT-I ⁴²	3991	451	23
CIBIS-II ⁴³	2647	515	20
COPERNICUS ⁴⁴	2287	465	28
BEST ⁴⁵	2708	593	22
Val HeFT ⁴⁶	5010	1002	20
RALES ⁴⁷	1663	446	27
SAVE ⁴⁸	2231	390	29
TRACE ⁴⁹	1749	501	22
CHARM ⁵⁰	7599	243	32
SCD HeFT ⁵¹	2521	580	23
DIG ⁵²	6800	1520	22.4
EPHESUS ⁵³	6642	1918	28.8
A-HeFT ⁵⁴	1050	420	40
CARE-HF ⁵⁵	813	216	26.5

Cardiovascular Disease in Women (V)

Heart Failure. Are Women Different?

María G. Crespo Leiro and María J. Paniagua Martín

Rev Esp Cardiol 2006



Femmes: moins incluses dans les registres?

Pourquoi être inclus dans un registre est important?

European Society of Cardiology Heart Failure Long-Term Registry (ESC-HF-LT): 1-year follow-up outcomes and differences across regions

Association between enrolment in a heart failure quality registry and subsequent mortality—a nationwide cohort study



Table 2 Demographics and other basal characteristics of the study population completing the 1-year follow-up

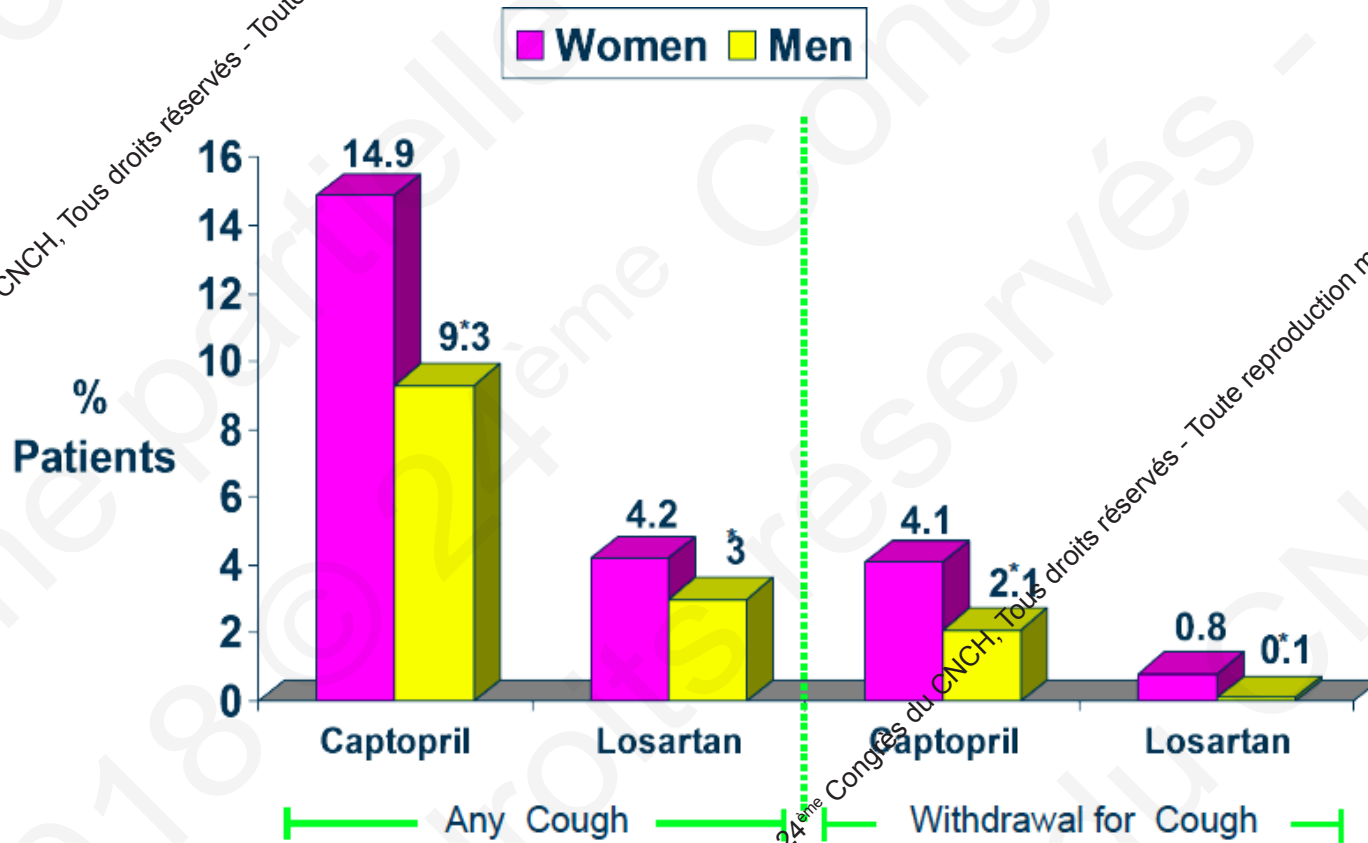
	AHF n= 4449	CHF n= 7173	P-value
Age (years)			
Mean ± SD	69.35 ± 12.98	64.89 ± 13.30	<0.0001
Median [IQR]	71 [61–79]	66 [57–75]	<0.0001
≥75 years, %	38.9	26.0	<0.0001
Females, %	37.4	28.8	<0.0001

37.4% in AHF
28.8% in CHF

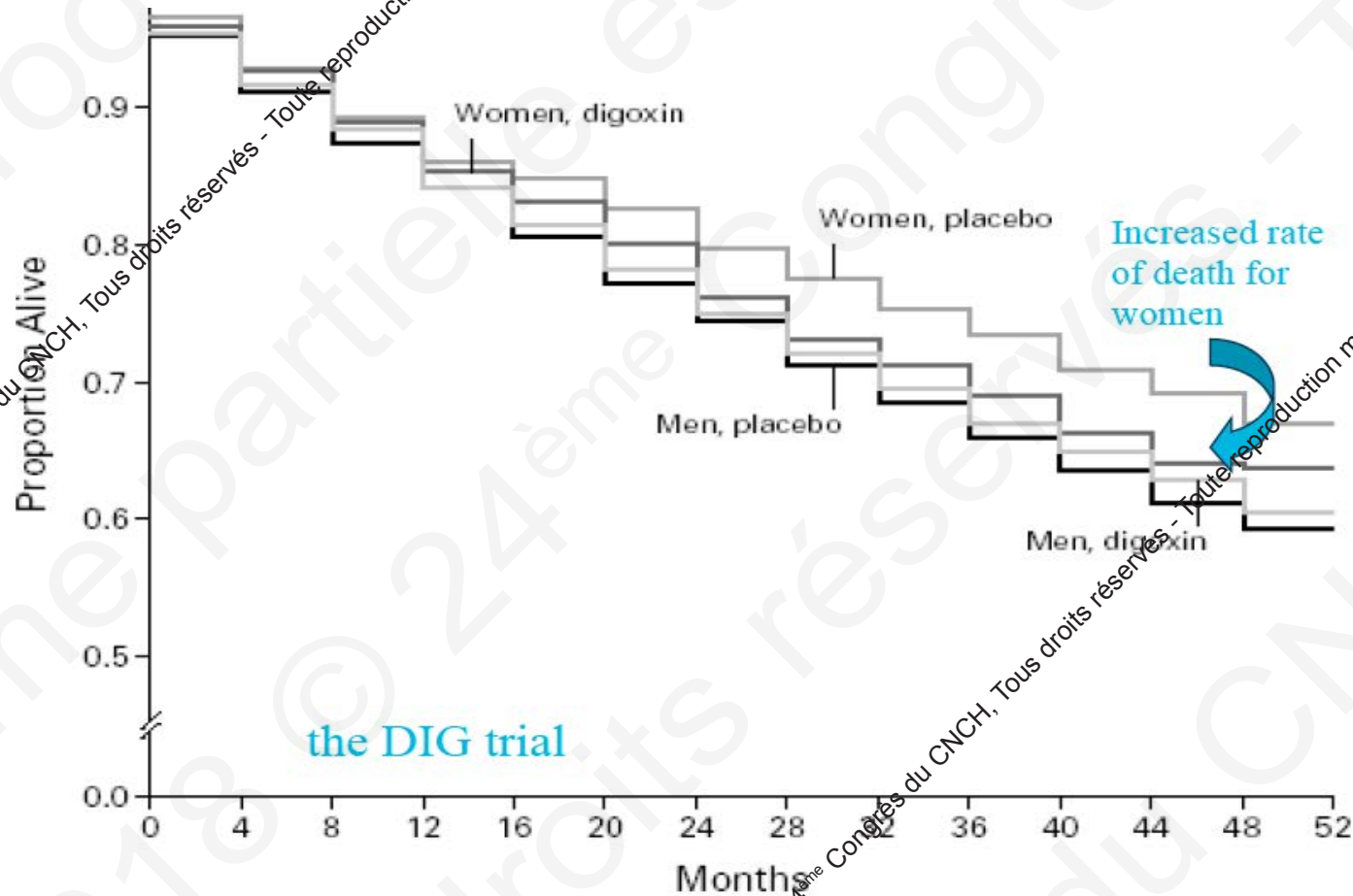
- Nation-wide prospective cohort study
- New-onset HF patients registered at Swedish National Patient Registry (NPR- mandatory ICD-code diagnosis) with or without concurrent registration in the Swedish HF Registry (SwedeHF- voluntary quality reporting registry)
- 2003-2016
- **231.437** patients included NPR; **21.888** (9.5% SwedeHF)
- Enrolment in a HF quality registry was associated with reduced all-cause mortality
 - explained by demographic differences and better utilization of cardiovascular and HF medications.

Femmes: moins bien traitées?

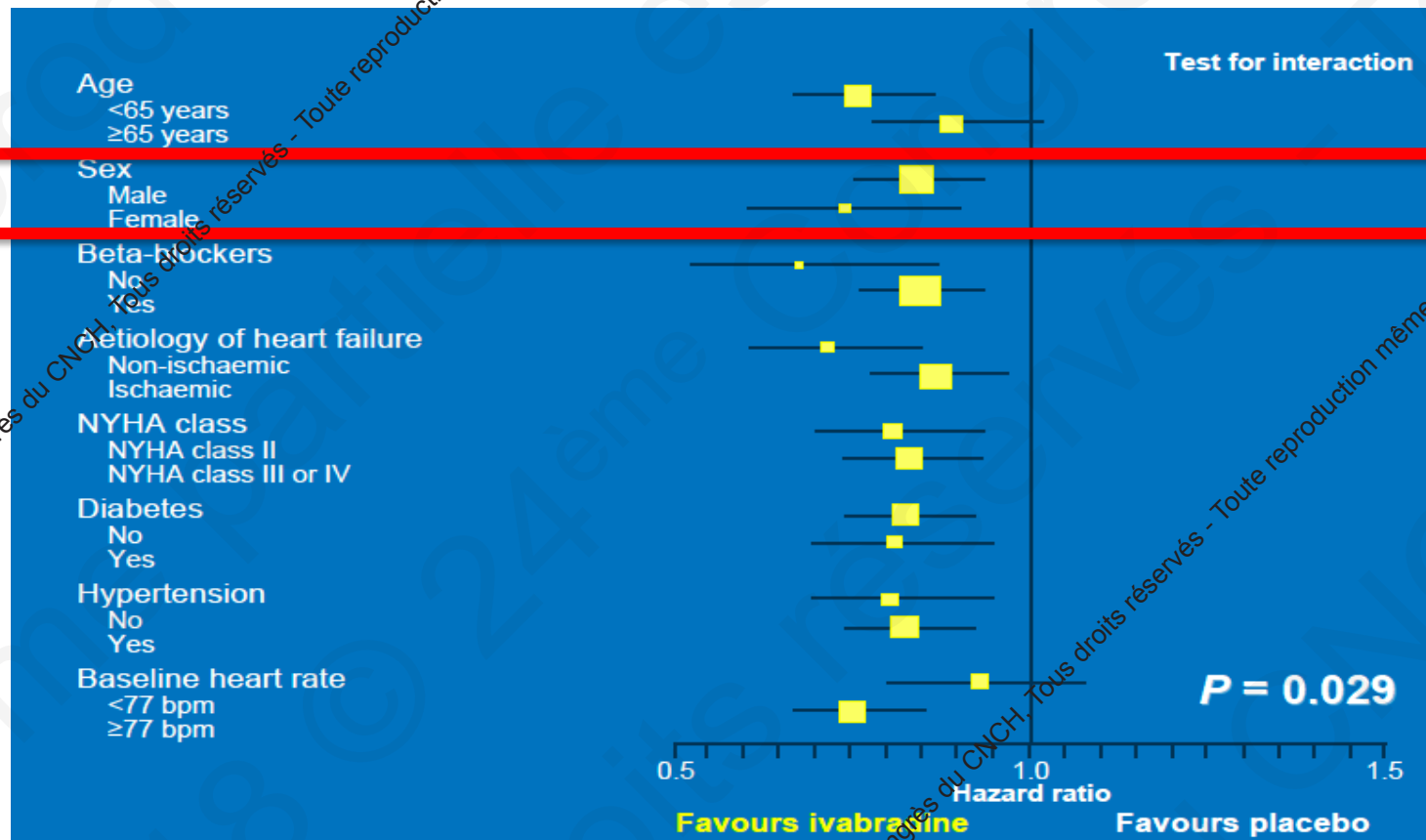
Toux secondaire aux IEC moins fréquente chez les femmes (ELITE II)



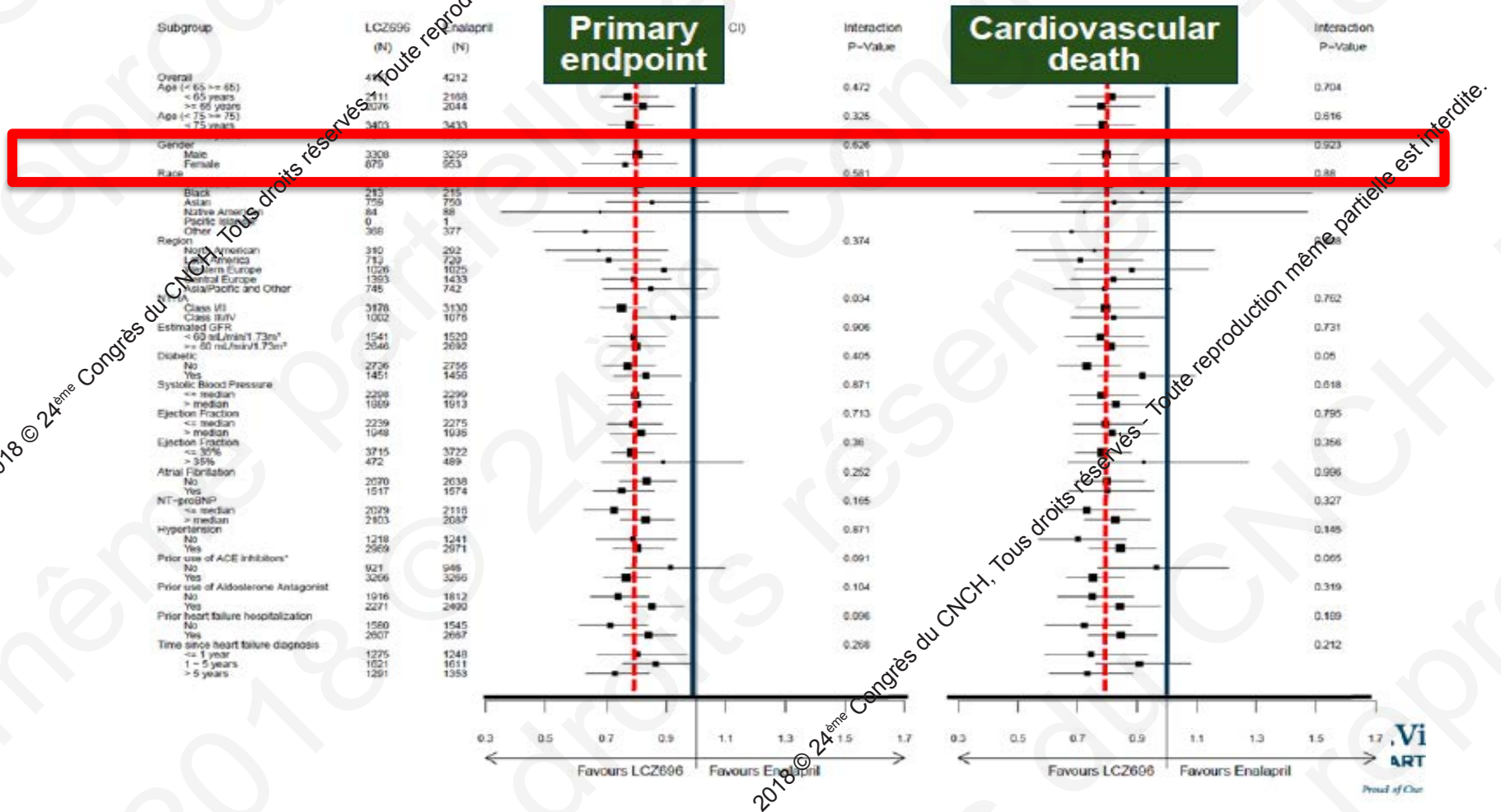
Taux de mortalité sous Digoxine plus élevé chez les femmes



Ivabradine chez les femmes



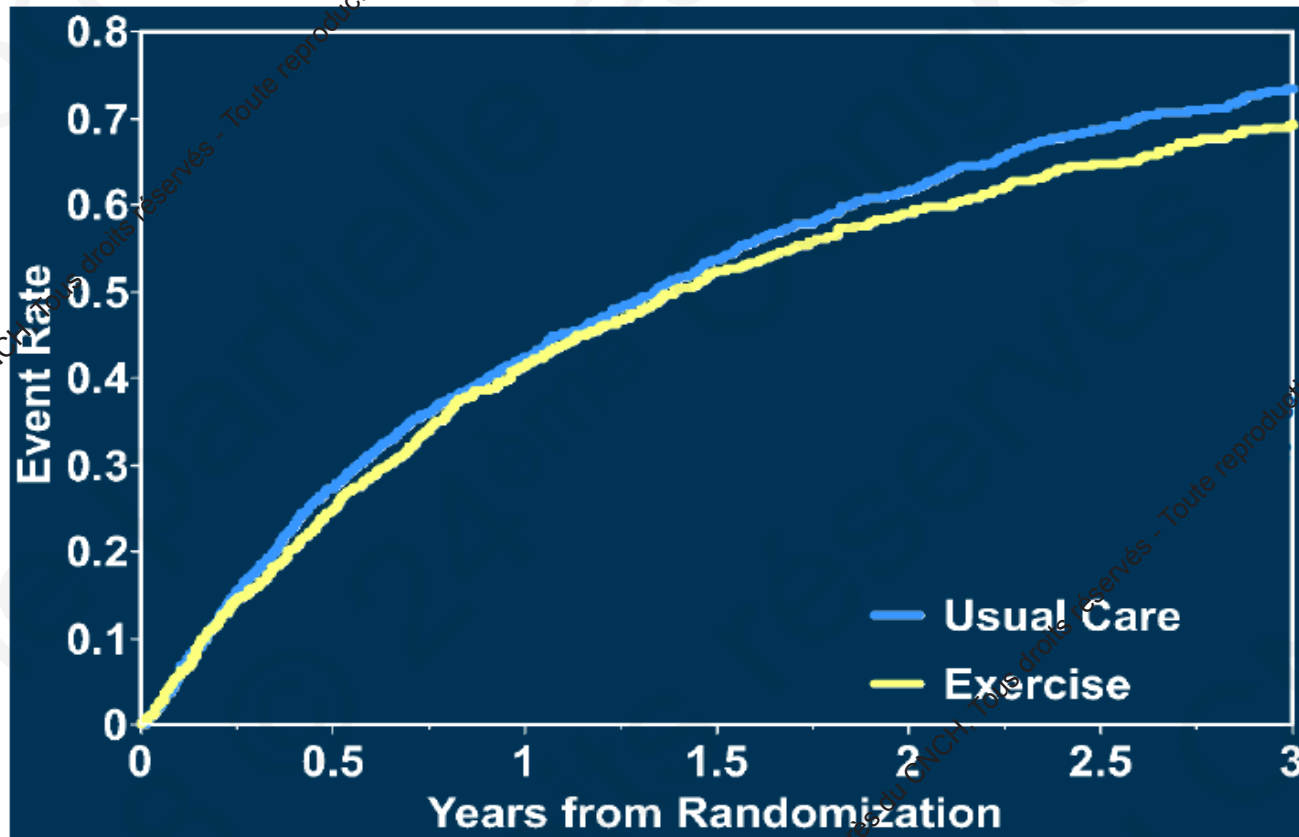
LCZ696 vs Enalapril sur le critere primaire et mortalité cardiovasculaire (sous-groupes)



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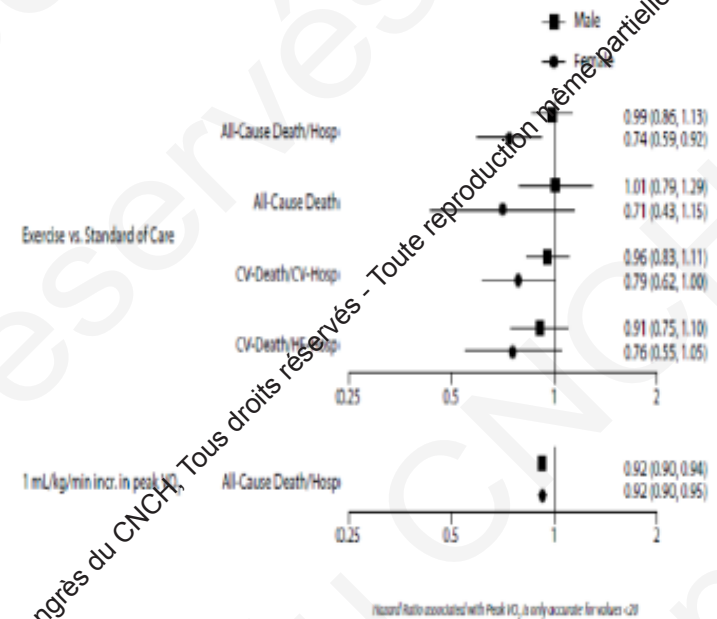
Toute reproduction même partielle est interdite.

HF-ACTION: mortalité toutes causes et hospitalisation toutes causes



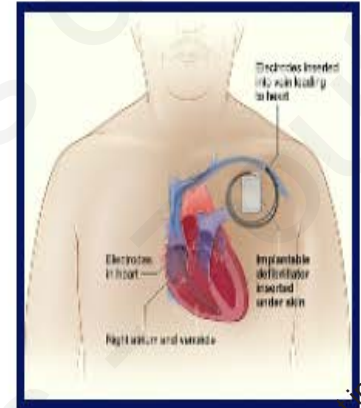
HF-ACTION Résultats selon sexe

- Exercise training in women with HF is associated with a reduction in the combined endpoint of all cause mortality and hospitalizations to a greater extent than in men
- A significant risk reduction was noted among women randomized to exercise training (HR 0.74, 95% CI 0.59-0.92), and virtually no risk reduction in the men (HR 0.99, 95% CI 0.86-1.13)
- Women have significantly lower values of Peak VO_2 than men and experience a non-significantly greater increase in Peak VO_2 after 3 months of treatment.



Sex and Race/Ethnicity Differences in Implantable Cardioverter-Defibrillator Counseling and Use Among Patients Hospitalized With Heart Failure

Findings from the Get With The Guidelines-Heart Failure Program



Observational analyses GWTG (2011-2014). N=21,059 patients

Patients admitted HFrEF (EF \leq 35%) without an ICD

- Rates of ICD counseling among eligible patients
- ICD receipt among those counseled

Women were counseled less frequently than men (19.3% vs 24.6%, $P < 0.001$)

Among those counseled women & men similarly likely to receive an ICD

Différence de réponse à CRT liée à sexe

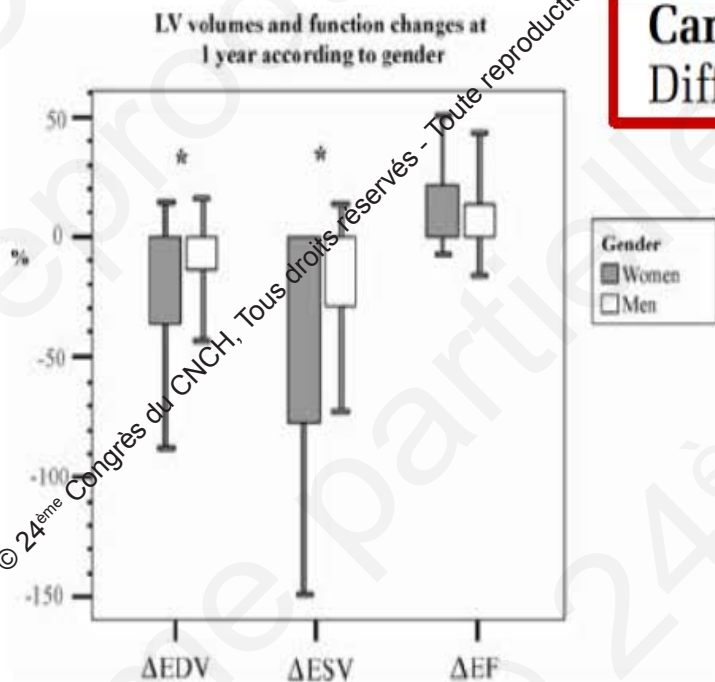
Etudes observationnelles

Les femmes par rapport aux hommes ont:

- Taux plus élevé d'IC non-ischémique, BBGC, complications péri procédurales
- Taux plus bas de FA et cardiopathie ischémique
- Volumes VG plus petits
- Sexe féminin est souvent un prédicteur indépendant de meilleure réponse à la resynchronisation (après ajustement avec la cause d'IC, largeur de QRS, FA et volumes du VG)

Meilleure réponse à la resynchronisation chez les femmes

Cardiac Resynchronization Therapy: Gender Related Differences in Left Ventricular Reverse Remodeling



334 HF CRT (19.7% women)

At 12 month FU, proportion of responders (ESV reduction by at least 10%) was greater in women 76.1% vs 59.3% ($p < 0.05$)

Figure 1. Changes in LV volumes and function from baseline to 12 months. Women show significant greater LV EDV and ESV reduction with no significant different change in LV EF. * $P < 0.01$ between men and women. Δ EDV = Delta End Diastolic Volume; Δ ESV = Delta and Systolic Volume; Δ EF = Delta Ejection Fraction.

CRT induced a gender-specific LV remodeling response

Left Bundle Branch Block Predicts Better Survival in Women Than Men Receiving Cardiac Resynchronization Therapy

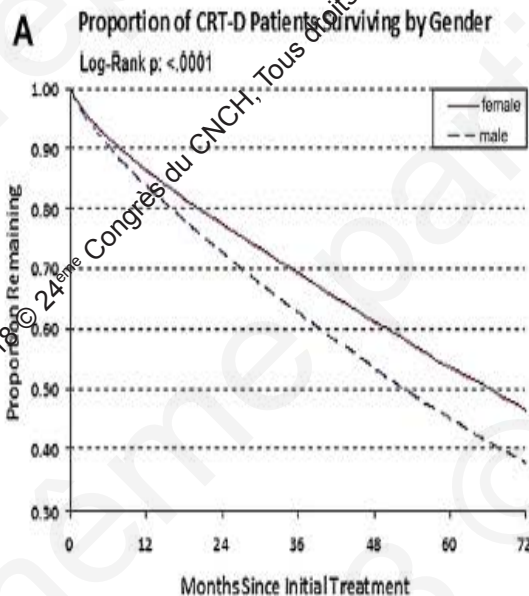
Long-Term Follow-Up of ~145,000 Patients

US Medicare recipients CRT-D (2002-2008)

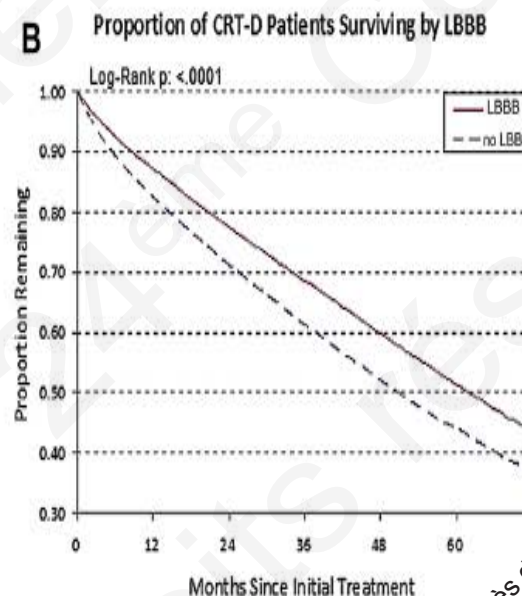
26% females

LBBB predicts better outcome in women than men

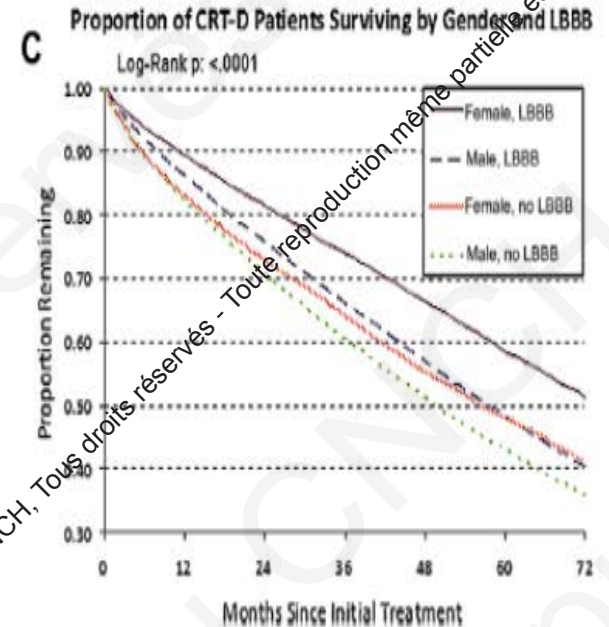
CRT Survival by Gender



CRT Survival by LBBB



CRT Survival by Gender & LBBB

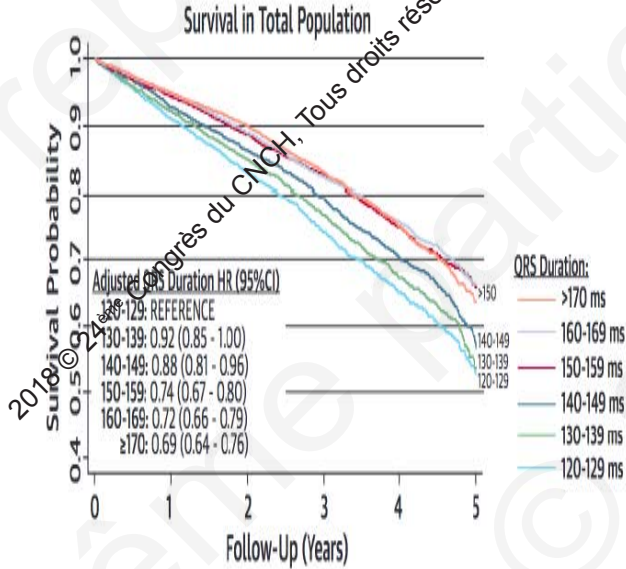


**BBGC associé avec la mortalité toutes causes plus basse chez les femmes
26% vs 15% p<0.01**

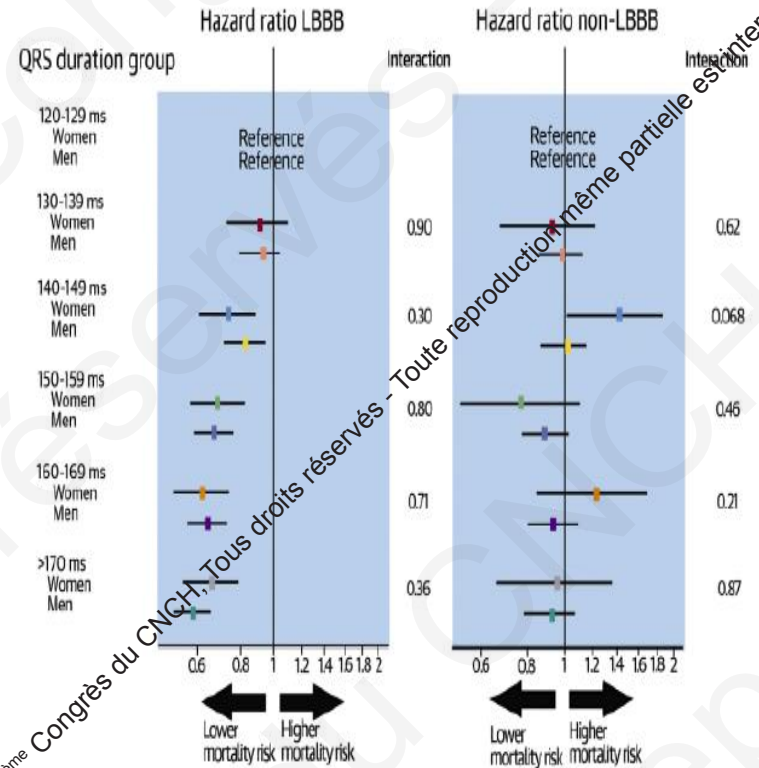
Sex-Specific Mortality Risk by QRS morphology and duration in Patients receiving CRT

31 892 CRT-D patients (36 % femmes)

NCDR National Cardiovascular Data Registry



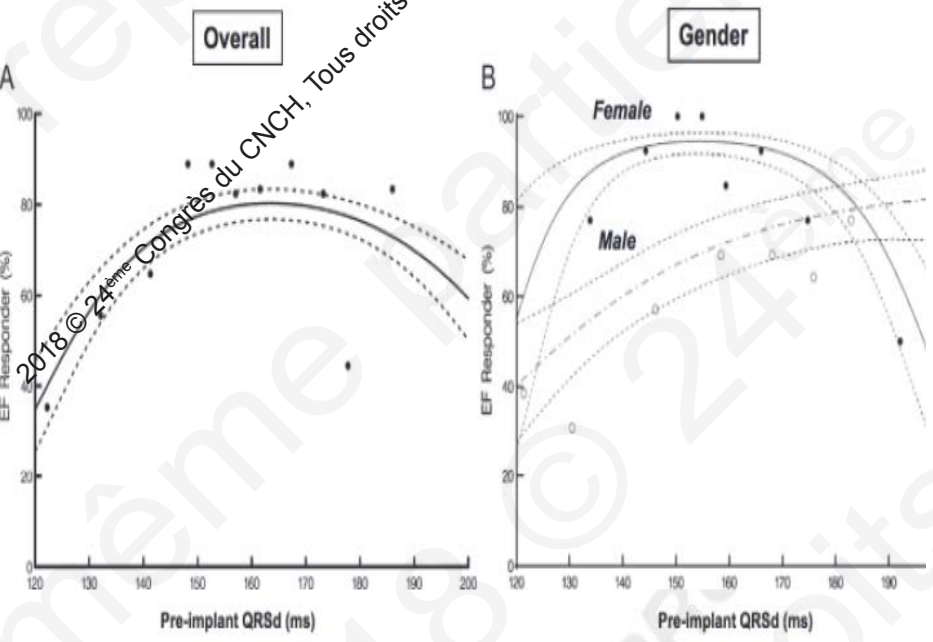
Probability of CRT survival
In 10 ms QRS duration groups



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Probability and magnitude of response to cardiac resynchronization therapy according to QRS duration and gender in nonischemic cardiomyopathy and LBBB

Probability of CRT Response According to QRS Duration



BBGC et cardiopathie non-ischémique
 Réponse + CRT → FE VG

N=212

CRT + : 71%

Meilleure réponse chez les femmes
84% vs 58% p < 0.001

QRSd < 150 ms vs ≥ 150 ms

Femmes: 86% vs 83% p=.77

Hommes: 36% vs 69% p<0.001

Assistance circulatoire mécanique

Femmes ont la même bénéfice au terme de survie que les hommes après une implantation d'assistance

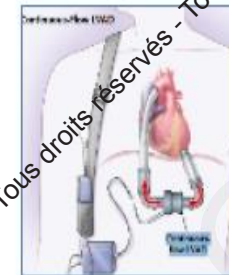
VG

- Étude HeartMate II BTT
- Etudes monocentriques
- Etude ADVANCE HVAD BTT
- Données INTERMACS ne montrent pas les différences en fonction de sexe pour les dispositifs pulsatiles (P=0.82) ou avec un flux continu (P=0.95)

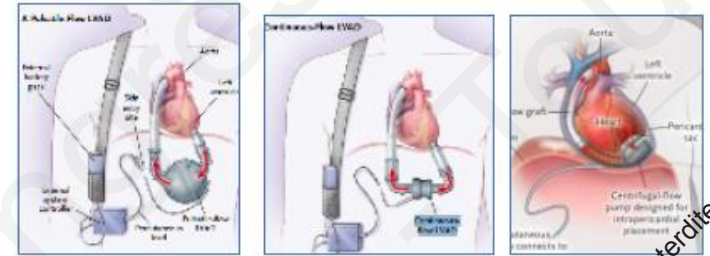
Assistance mécanique circulatoire: inclusion des femmes dans les études < 30%

Device (clinical trial)	Year	Women	Sex-specific outcome data
HeartMate IP (BTT)	1992	3 % HeartMate IP	No [78]
HeartMate XVE (BTT)	2001	17 % HeartMate XVE	No [79]
HeartMate XVE (DT)	2001	22 % HeartMate XVE	No [81]
AbioCor TAH (feasibility)	2004	0 % AbioCor	No [77]
CardioWest TAH (BTT)	2004	14 % CardioWest	No [76]
Novacor (BTT)	2007	18 % medical therapy 8 % Novacor	No [80]
HeartMate II (BTT)	2007	28 % medical therapy 21 % HeartMate II	Yes [75]
HeartMate II (DT)	2009	19 % HeartMate II	No [82]
HeartWare HVAD (BTT)	2015	8 % HeartMate XVE 28 % HeartWare 24 % INTERMACS control	Yes [74]

IP implantable pneumatic, *BTT* bridge to transplantation, *DT* destination therapy, *INTERMACS* Interagency Registry for Mechanically Assisted Circulatory Support, *TAH* total artificial heart, *XVE* vented electric



Femmes et assistance mécanique circulatoire



Particularités anatomiques (beaucoup de femmes sont trop petites pour recevoir une assistance ventriculaire)

- **Assistance ventriculaire pulsatile**

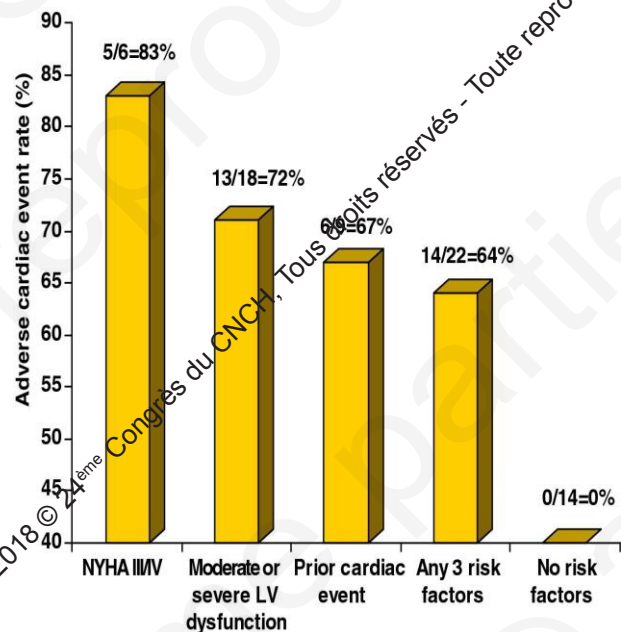
Mortalité élevée, moins susceptibles de recevoir un greffe cardiaque, plus mauvais survie post-greffe par rapport aux hommes

- **Assistance ventriculaire avec un flux continu a un survie similaire parmi les hommes et les femmes, mais:**

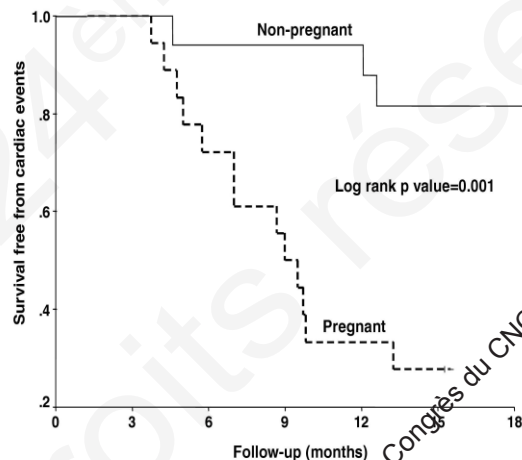
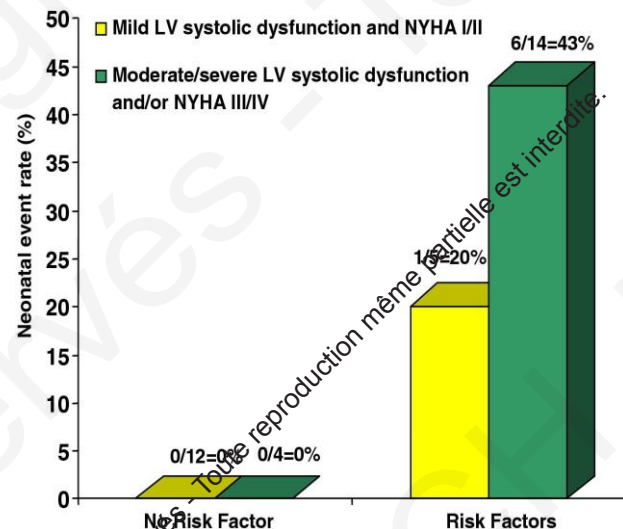
Femmes adressées plus tard avec IC plus avancée et risque plus élevé d'insuffisance VD, complications neurologiques et rénales

Comparaison des évènements cardiaques chez les femmes avec la dysfonction systolique du VG, pendant la grossesse et en fonction de l'âge et FE VG

Incidence of adverse cardiac events according to maternal risk factors



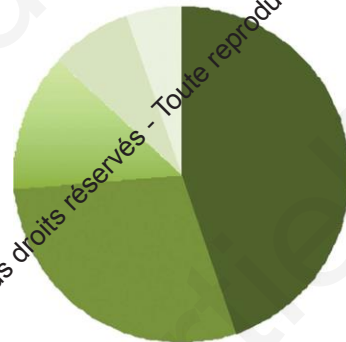
Frequency of neonatal events in women with vs without risk factors



No. at Risk	0	3	6	9	12	15	18
All	36	36	31	28	24	21	20
Pregnant	18	18	14	11	6	6	5
Non-pregnant	18	18	17	17	17	15	15

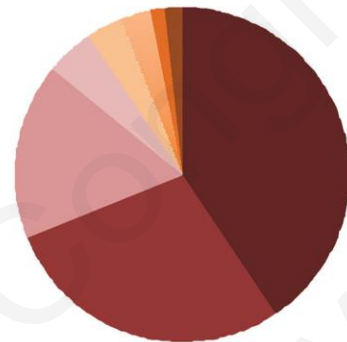
28 vs 83 %

Diagnosis in Patients with HF-Data from Registry of Pregnancy and Cardiac Disease (ROPAC)



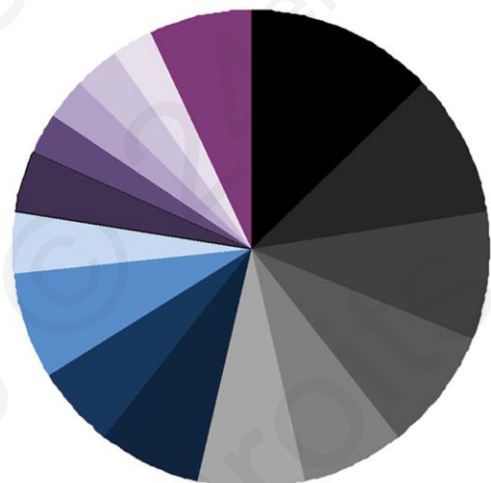
- Peripartum cardiomyopathy/myocarditis
- Dilated cardiomyopathy
- Hypertrophic non obstructive cardiomyopathy
- Hypertrophic obstructive cardiomyopathy
- Cardiomyopathy other
- ischemic heart disease

Cardiomyopathie =36



- Mitral stenosis
- Mitral regurgitation
- Mitral stenosis and regurgitation
- Aortic regurgitation
- Aortic stenosis and aortic regurgitation
- Pulmonary stenosis
- Aortic stenosis
- Tricuspid regurgitation

Maladie valvulaire=64



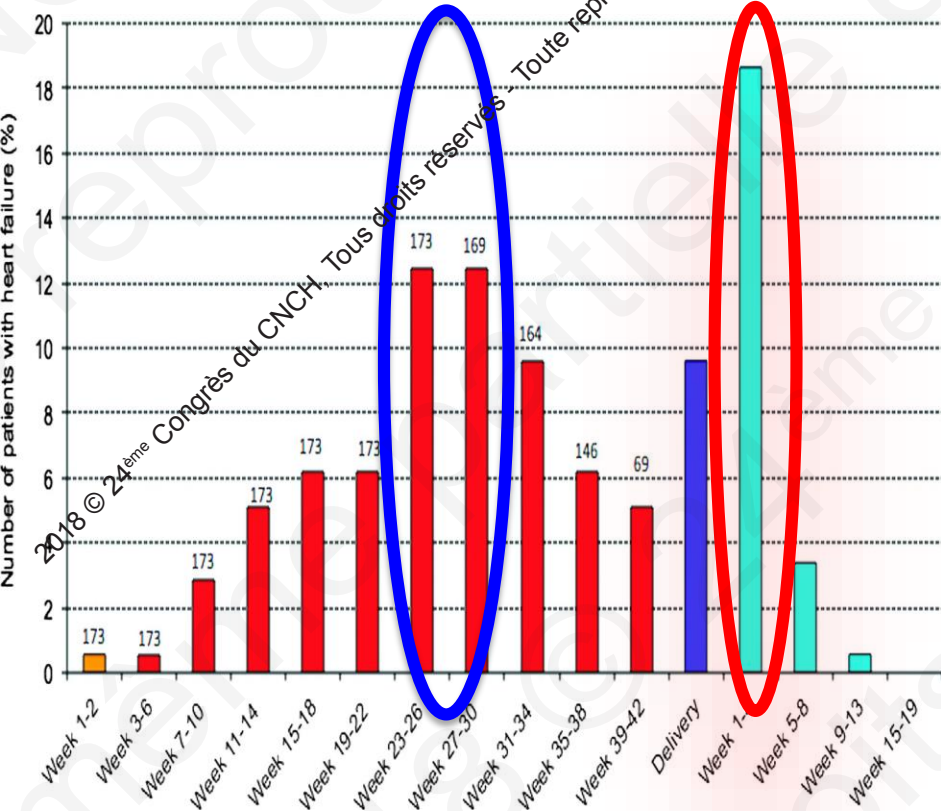
- ASD
- PDA
- Aortic coarctation
- Aortic abnormality
- Tetralogy of fallot
- VSD
- AVSD
- Pulmonary valve abnormality
- Double outlet right/left ventricle
- Mitral valve abnormality
- Transposition of the great arteries
- Marfan's syndrome
- Pulmonary vein abnormality
- PFO
- Pulmonary artery dilatation
- Other

Cardiopathie congenitale=71

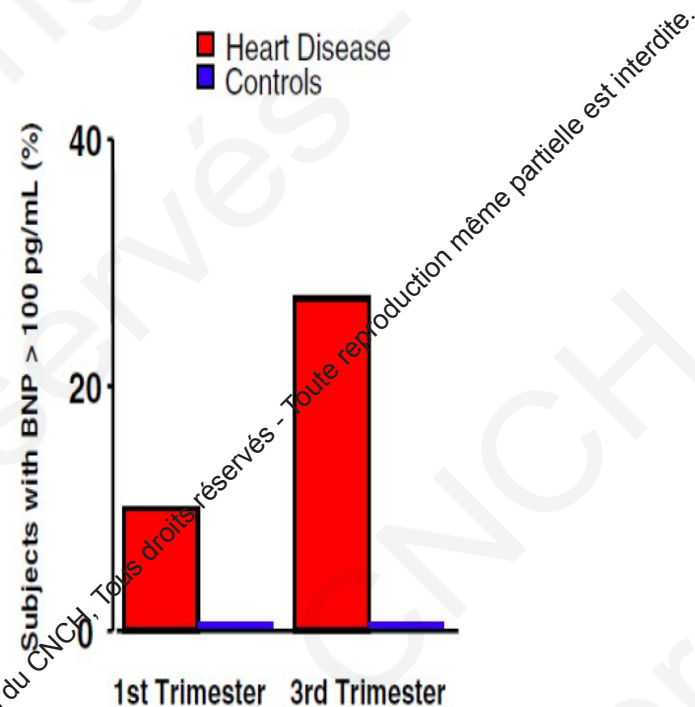
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Timing of HF Onset Group

Data from the Registre on Pregnancy and Cardiac Disease (ROPAC)



Elévation significative de BNP pendant la grossesse



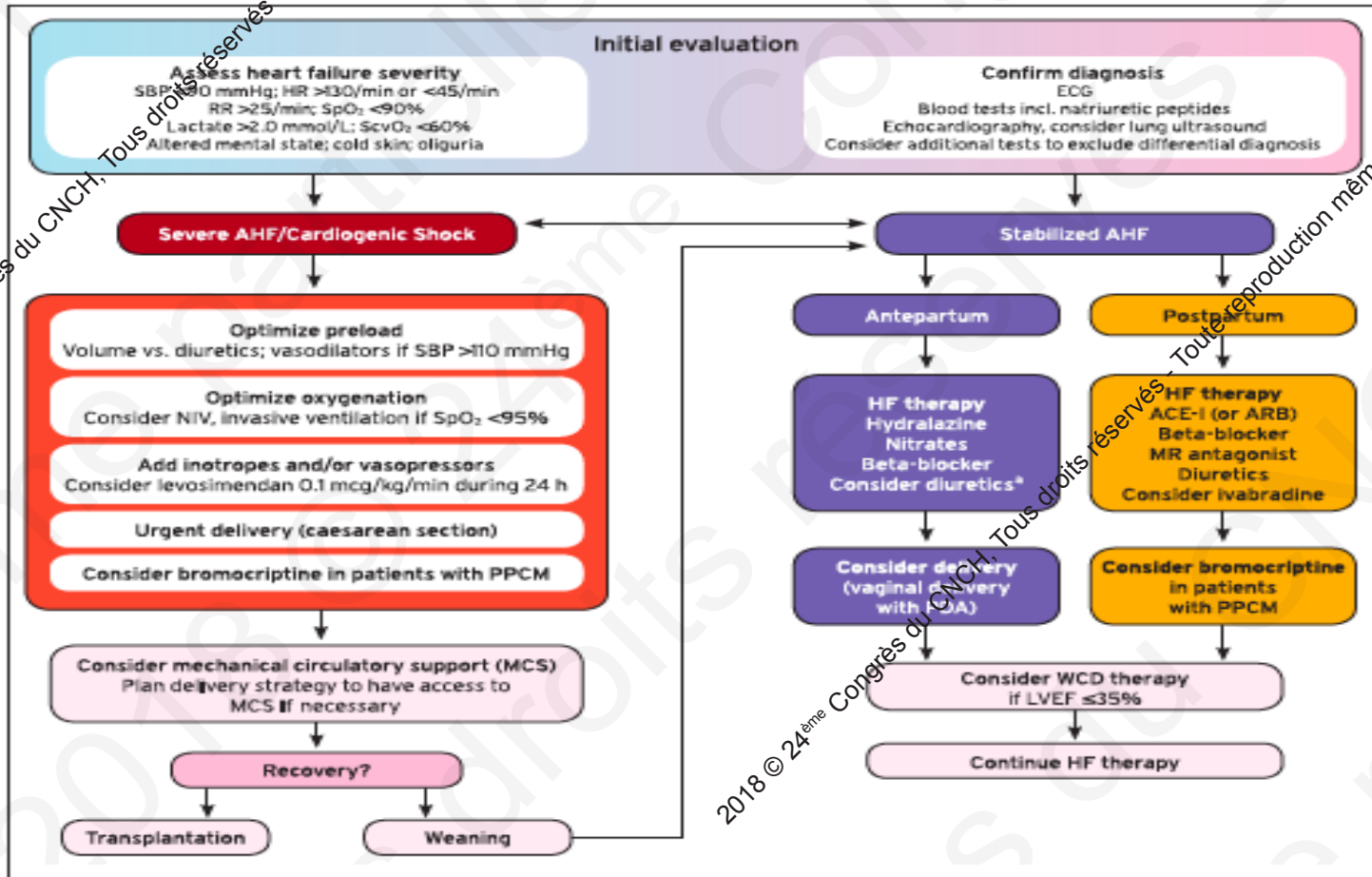
Traitement d'ICC pendant la grossesse

Drug/Class	Purpose	Comment
DIURETICS		
Furosemide	Generally reserved for Rx of PE Use lowest possible dose	Placental hypoperfusion Contraindicated in IUGR, pre-eclampsia; FDA class C
DIGOXIN	Useful in pregnancy, given limited Rx	Safe; Useful for persistent HF symptoms; FDA class C
VASODILATORS		
Hydralazine	Used to substitute for ACEI	Effective in pregnancy-related HTN Risk of hypotension, as pregnancy already reduces SVR Avoid large doses; FDA class C
ACEI/ARB	Decrease in M&M in non pregnant women	Contraindicated throughout pregnancy due to teratogenic effects (oligohydramnios, neonatal death due to RF, renal agenesis); FDA class C 1 st Trim; D thereafter
Amlodipine	Alternative to ACEI in pregnancy	Can be used with hydralazine if needed; FDA class C
Nitrates	Useful in ADHF	FDA class C
BETA Blockers	Essential in HF Rx B-1 selective preferable Should be continued throughout preg.	Safe and effective in preg.; Can cause IUGR Infants should be observed for 72 h after birth FDA class C
SPIRONOLACTONE	Increases survival in HF Not routinely used in preg.	No data to support safety in preg.; FDA class D
WARFARIN	Risk/benefit ratio must be discussed with pt.	1 st trimester teratogenesis Dosing complicated in preg.; FDA class X

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2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy



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Timing et mode d'accouchement

- Décubitus latéral gauche
- Accouchement court par voie basse avec la possibilité d'assistance en 2nd période d'accouchement
- Césarien en fonction des indications obstétriques
- Surveillance invasive de l'hémodynamique si nécessaire
- Traitement médical afin d'améliorer les conditions de charge
- Monitoring et TT rapide d'OAP

PEC en post-partum

- Détecter et traiter une anémie
- Traitement médical pour optimiser les conditions de charge (traitement d'OAP)
- Télémétrie et monitoring de l'état hémodynamique 12-24h
- Considérer contraception et stérilisation
- Considérer DAI

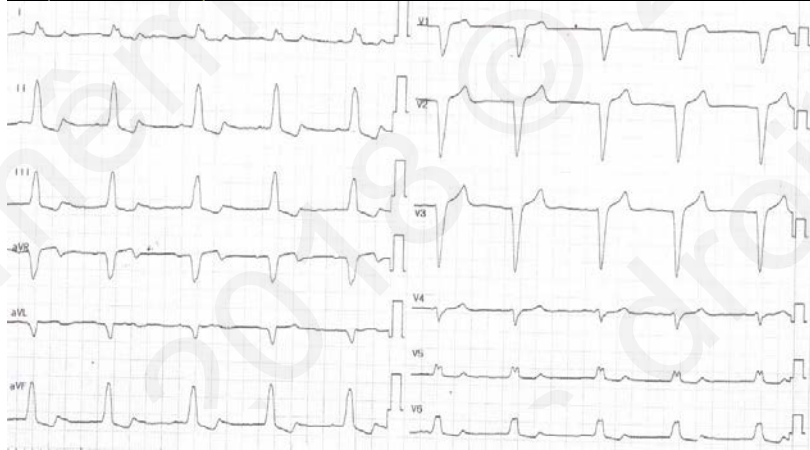
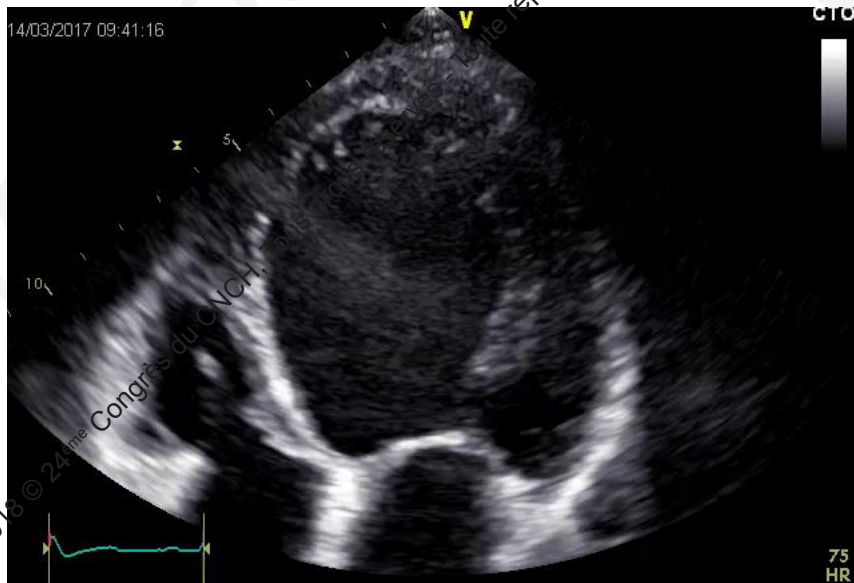
Take home message

- Maladies CV c'est la 1ere cause de mortalité chez les femmes
- Les femmes avec IC sont plus âgées et ont la plus haute pourcentage d'IC FEP
- On a besoin inclure plus de femmes dans les études cliniques et registres
- Même si elles ont moins représentées dans les études cliniques, les données montrent que les femmes ont plus de bénéfice de thérapie de resynchronisation que les hommes
- ACM avec flux continu a la même bénéfice chez les hommes et les femmes
- IC est une complication la plus fréquente chez les femmes enceintes avec des maladies cardiaques avec la mortalité maternelle et foetale élevée

Trouvez les différences...

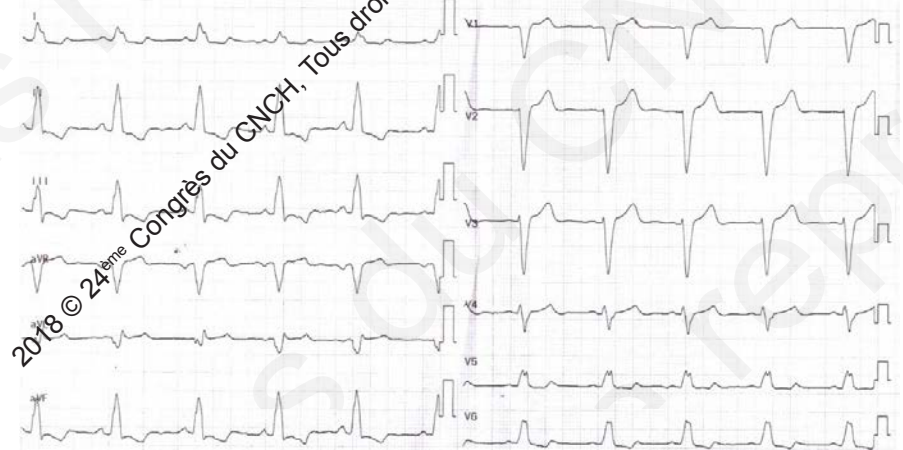
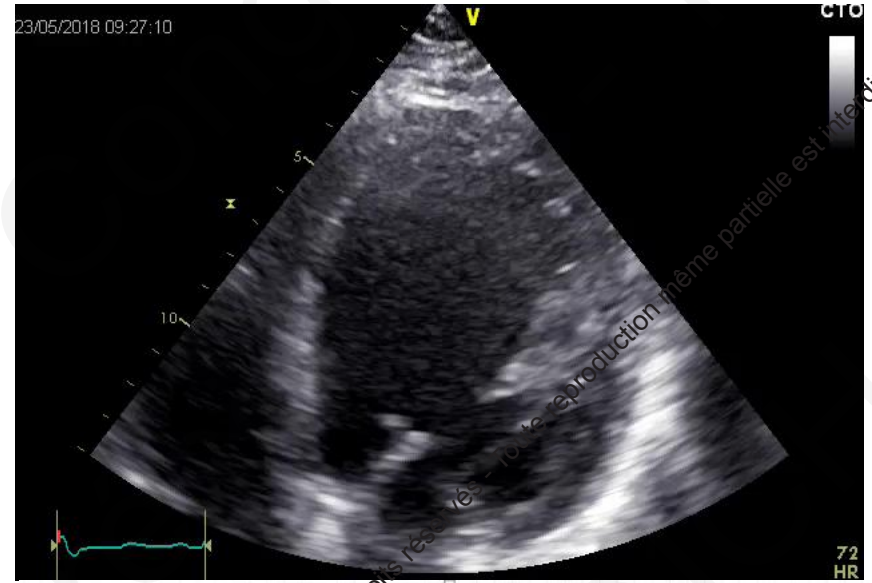
Patient 1, âge 50 ans
CMD non -ischémique

Avant CRT-D, FE VG 35%, QRS 152 ms, BBGC



Patient 2, âge 52 ans
CMD non-ischémique

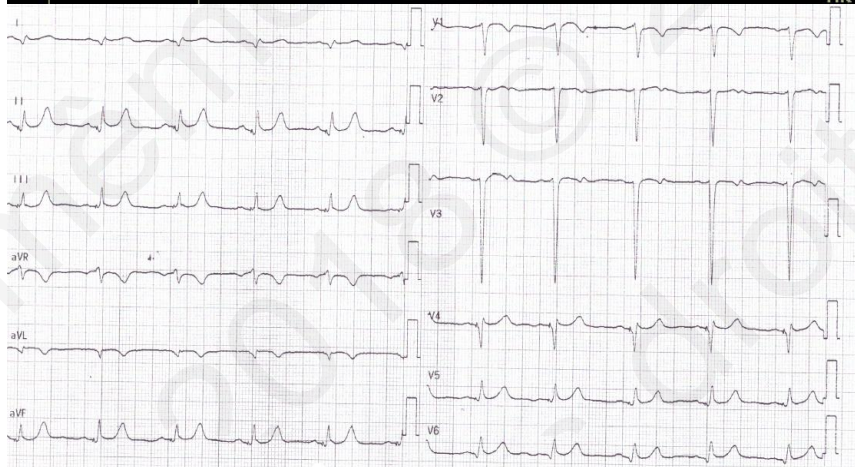
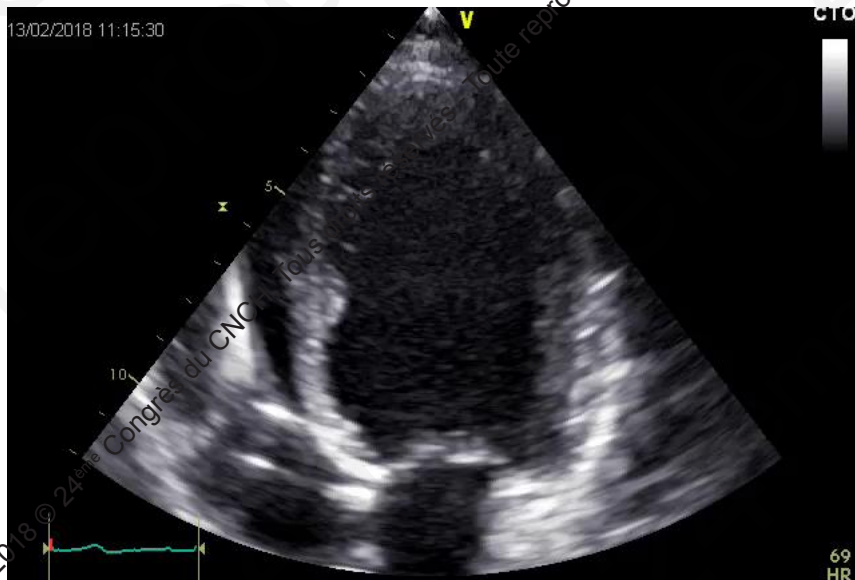
Avant CRT-D, FE VG 33 %, QRS 154 ms



Trouvez les différences...

Patient 1, 50 ans

Après CRT-D, FE VG 52 % QRS 102 ms



Patient 2, 52 ans

Après CRT-D, FE VG 50 %, QRS 135 ms

