

Updates in Hospital Medicine

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DATE: November 13th, 2021

1

Updates in Hospital Medicine 2020 - 2021

No Conflicts of Interest

2

2

Updates in Hospital Medicine 2020 - 2021

Objectives

- Review and evaluate recent impactful literature in the practice of Hospital Medicine
- Develop a plan for how this data may: confirm, inform, or perhaps change your practice
- Save you some time and keep you entertained

3

3

Updates in Hospital Medicine 2020 - 2021

Road Map

- New literature from 2020-2021
- No COVID-19 studies
- High level review
 - Case based approach
 - Mix of “quick takes” and deeper dives
- Articles selected based on likelihood to:
 - ✓ Change practice
 - ✓ Inform/Modify practice
 - ✓ Confirm practice

4

4

Change in Heart Failure Paradigm

67 yo Female w hx of HTN, CAD, and CHF (EF 55%) p/w 1 week DOE, LE swelling, orthopnea admitted with a heart failure exacerbation.

Diuresed well and is nearing discharge.

Current Meds: Metop, Sacubitril/Valsartan, Aldactone, Atorva, ASA, and Furosemide.

- a) You start a low dose of Empagliflozin/Dapagliflozin
- b) Defer start of SGLT-2i once stable to PCP/Cardiologist given recent exacerbation
- c) You hold off given questionable benefit of SGLT-2i when on ANRI/MRA
- d) You lobby your hospital admin to put SLGT2i in the water supply.

5

5

SLGT-2i: What to make of them

- Several important studies within the last year for Heart Failure
 - DAPA-HF (2019)
 - EMPEROR-Reduced (2020)
 - Meta-analysis of DAPA-HF
EMPEROR-reduced (2020)
 - **EMPEROR-Preserved (2021)**



6

Back ground: HFrEF

- DAPA - HF and EMPEROR-Reduced
 - Large Double Blinded RCTs of Dapagliflozin/ Empagliflozin vs Placebo in HFrEF (EF<40%)
 - ~25% RR reduction in HF hospitalization/CV mortality
 - ~15% RR in all cause mortality in Meta Analysis
 - ~30% RR reduction in progression of CKD
 - Independent of DM status
 - Consistent in Subgroups of MRA, ARNI

McMurray et al NEJM Nov 2019, Packer et al NEJM Oct 2020, Zannad et al Lancet Aug 2020

7

EMPEROR-Preserved

- Large, RCT of Empagliflozin vs Placebo in HFpEF
 - n=5988
 - >18 yo, Dx of HFpEF EF >40%, NYHA II-IV
 - BNP >300, >900 if dx Afib
 - Median LVEF 54%, 2/3 LVEF >50%
 - 1° Outcome: HF Hospitalization or CV Death
 - 2° Outcome: Progression of Renal disease
 - ~26 month median follow up

Anker et al NEJM Aug 27th 2021

8

EMPEROR-Preserved

	Empagliflozin (n=2997)	Placebo (n=2991)	HR (95% CI)	P value
Composite HF Hosp/CV Death	415	511	0.79 (0.69-0.90)	<0.001
HF Hospitalization	259	352	0.71 (0.60-0.83)	
Cardiovascular Death	219	244	0.91 (0.76-1.09)	
eGFR Mean Change	-1.25	-2.62	1.36 (1.06-1.66)	<0.001

- ~20% relative risk reduction, NNT=31
- Reduction in progression of renal disease

Anker et al NEJM Aug 27th 2021

9

EMPEROR- Not so preserved

- 49% had DM, ~15% on ACEI, ARB, ARNI
 - No difference in subgroups

- Effect appeared to be LVEF dependent
 - Benefit lessened with higher EF
 - No benefit for >60%

	HR (95% CI)
DM II	0.75 (0.63-0.90)
No DM	0.73 (0.60-0.88)
ARNI	0.80 (0.69-0.93)
No ARNI	0.75 (0.57-0.99)

LVEF (n%)	HR (95% CI)
<50% (33.2)	0.75 (0.57-0.88)
50%-60% (34.3)	0.80 (0.64-0.99)
>60% (32.5)	0.87 (0.69-1.10)

Anker et al NEJM Aug 27th 2021

10

SLGT2i in HF: Take Aways

- Caveats:
 - Primary Outcome driven largely by HF Hospitalization
 - Majority of benefit in patients with EF <60%.
 - Similar seen in ARNI study in HFpEF
- Take Away: SGLT2i use in patients with HFrEF and HFpEF* (EF <60)
 - Now part of GDMT
 - Safe to initiate inpatient once stable prior to discharge

Change my practice towards more IP prescribing of SGLT2i for patients with heart failure exacerbations for patients with EF <60%.

11

Change in Heart Failure Paradigm

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12

12

Quick Take: SGLT-2, first DMII, HF, and now CKD??

- RCT of 4304 pts with CKD (eGFR 25-75, Alb/Cr 200-5000) to Dapagliflozin or Placebo
 - Primary Outcome: Loss of at least 50% of eGFR, ESRD, or Death
 - ~ 67% had DM and ~11% had HF
 - Median follow up 2.4 yrs

	Dapagliflozin (n=2152)	Placebo (n=2152)	HR (95% CI)	P value
50% loss eGFR, ESRD, Death	197	312	0.61 (0.51-0.72)	<0.001
All Cause Mortality	101	146	0.69 (0.53-0.88)	0.004

Diabetes	HR (95% CI)
Yes	0.64 (0.52-0.79)
No	0.50 (0.35-0.72)

Heerspink et al NEJM October 2020

13

Quick Take: SGLT-2, first DMII, HF, and now CKD??

- Significant implications for treatment of CKD in the outpatient setting.

Bottom Line: Unlikely to change inpatient prescribing but we will be seeing this.

Heerspink et al NEJM October 2020

14

What about IV Iron?

Back to our patient: 67 yo Female w hx of HTN, HLD, CAD, and HF (EF45) with a heart failure exacerbation.

Ferritin sent on admission is 70. Hgb 13.4

- a) Patient isn't anemic so no benefit for iron repletion
- b) Prescribe PO Iron... and some laxative
- c) Given IV iron on discharge and encourage follow up iron studies with PCP/Cardiology
- d) Why did someone check a Ferritin, I don't want to deal with this

15

What about IV Iron?

- RCT of 1108 pts hospitalized with acute HF exacerbation (EF <50%) and iron deficiency to IV iron vs placebo
 - Ferritin <100, or 100-299 & sat <20
 - Primary Outcome: HF hospitalization or CV death
 - Followed for 52 weeks
 - Patient Characteristics
 - Mean Hgb ~12
 - Mean LVEF 32%
 - <25% ->22%
 - 25-39 -> 44%
 - 40-49% 33
 - ~30% new dx CHF, ~28% with CHF hospitalization <12 mo

Ponikowski et al. Lancet Dec 2020

16

What about IV Iron?

	IV Iron (n=558)	Placebo (n=550)	HR (95% CI)	P value
HF Hosp/ CV Death	293	372	0.79 (0.62-1.01)	0.059*
HF Hospitalization	217	294	0.74 (0.58-0.94)	0.013
Pre-COVID: HF Hosp/ CV Death	274	363	0.75 (0.59-0.96)	0.024
Pre-COVID: HF Hospitalization	202	287	0.70 (0.55-0.90)	0.005

- Narrowly missed primary outcome
 - ~25% reduction in HF Hospitalization
- Pre-Covid Sensitivity Analysis showed significance in both outcomes

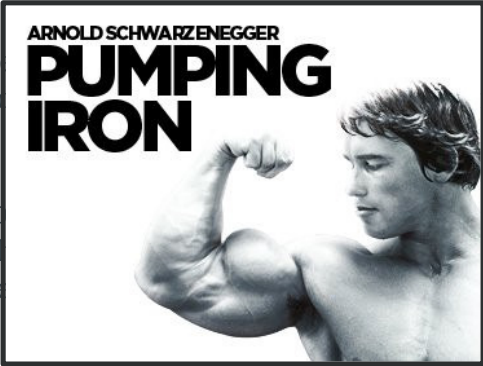
No difference in subgroup of Hgb >12

Ponikowski et al. Lancet Dec 2020

17

What about IV Iron?

- Caveats
 - Effect greater in OP setting.
 - Study included patients with iron deficiency
- Take Away: In HF patients with iron deficiency, IV iron has been shown to
 - Reduce HF Hospitalization
 - Mortality benefit



ARNOLD SCHWARZENEGGER
PUMPING IRON

Confirms practice of checking ferritin, TIBC in all HFrEF patients and giving IV iron prior to discharge if iron deficient

Ponikowski et al. Lancet Dec 2020

18

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19

Quick Take: Discharge before when?

- Multicenter retrospective cohort study in GIM patients to determine if AM discharge (before 12:00pm) decreased ED LOS or Hospital LOS
 - 7 Hospitals, 7 years, ~180,000 ED admissions
 - After multivariate analysis there was no association between AM discharges and Hospital LOS or ED LOS
- Caveat: One hospital system in Canada, One of 7 hospitals did have an association

Kirubarajan et al. J. Hosp. Med May 2021

20

Transfusion Threshold in Ischemia

56 yo Male with a hx of HTN, HLD, and GERD p/w acute chest pain in the setting of several days of melena.

- He is HD stable. EKG -> ST depressions and a Troponin trend c/w with an NSTEMI and ACS.
 - He is given ASA, Plavix, and Heparin w/ a plan for PCI in the morning. His Hgb is down to 8.5 from a baseline of 10-11.
- a) Transfuse pRBCs until Hgb >10
 - b) Wait and transfuse only if HD unstable or Hgb <8
 - c) Give IV iron because it seems to fix heart failure
 - d) Wait to see what Cardiology puts in their note

21

Transfusion Threshold in Ischemia

- Non-Inferiority trial of a Restrictive (Hgb <8) vs Liberal (Hgb <10) transfusion protocol in Acute Myocardial Infarction and Anemia.
 - Baseline Hgb 7-10
 - Primary Outcome: MACE (Death, CVA, rMI, emerg. PCI) within 30 days
 - ~29% STEMI, 71% NSTEMI
 - ~85% without active bleeding

	Restrictive n=342	Liberal n=324
Hgb Admission	10	10.1
Hgb Discharge	9.7	11.1
Units Transfused	342	748
FFP	2(0.9)	7 (2.2)
Platelets	4(1.2)	6(1.9)

Ducrocq et al JAMA Feb 2021

22

Transfusion Threshold in Ischemia

	Restrictive (Hgb<8)	Liberal (Hgb<10)	HR (97.5% CI)
MACE (as treated)	36/327	45/322	0.79 (0.00-1.19)
MACE (as randomized)	38/342	46/324	0.78 (0.00-1.17)

- Restrictive approach was non-inferior to liberal strategy
 - 25% allowable difference for Non-Inferiority

Ducrocq et al JAMA Feb 2021

23

Transfusion Threshold: Take Aways

- Caveats
 - CI for non-inferiority includes clinically relevant outcome of up to ~18% higher rates of adverse events
 - Majority were incidentally anemic (~85%)
- Take Away
 - High quality trial with effective differences in transfusions received and non-inferior point estimate for RR toward restrictive rather than liberal transfusion approach

Inform my practice toward a more restrictive approach for transfusion in AMI.

Ducrocq et al JAMA Feb 2021

24

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25

Inpatient Hypertension treatment

65 yo F w HTN, CKD, IDDM, and Hx of mechanical MV admitted with cellulitis. Done well on IV antibiotics with plans for early morning discharge before noon tomorrow.

You receive a page: Her blood pressure is 165/92. She is asymptomatic.

Hypertensive between 150-160/80-85 on home regimen of Lisinopril, and Amlodipine.

- a) Order 25 mg PO Hydralazine prn SBP >160
- b) Quit messing around an order 10 mg IV Labetalol
- c) Order 25mg Metoprolol Succ PO daily now and on discharge.
- d) Put in your headphones, find your Zen place, and do absolutely nothing

26

Inpatient Hypertension Treatment

Retrospective cohort study of 22,834 pts on the practices and outcomes of inpatient asymptomatic HTN treatment in non-cardiac hospitalization.

- Propensity Matching
- Exposure: Treatment of Asymptomatic HTN
- Composite Primary Outcome: Stroke, MI, AKI
- 17,821 patients, 106,097 episodes of HTN
 - 5904 pts (33%) and 8692 episodes (8.2%) treated
 - 5747(66%) with PO medications

Rastogi et al JAMA Internal Med Dec 2020

27

Inpatient Hypertension Treatment

	Unmatched No Treatment (n=11917)	Unmatched Treatment (n=5904)	P value	Matched No Treatment (n=4520)	Matched Treatment (n=4520)	P value
Composite Outcome	728 (6.1%)	738 (12.5%)	< 0.001	371 (8.2%)	499 (11.0%)	< 0.001
Stroke	10 (0.1%)	6 (0.1%)	0.92	4 (0.1%)	4 (0.1%)	> 0.99
Acute Kidney Injury	690 (5.8%)	690 (11.7%)	< 0.001	357 (7.9%)	466 (10.3%)	< 0.001
Myocardial Injury	51 (0.4%)	76 (1.3%)	< 0.001	26 (0.6%)	53 (1.2%)	0.003
Length of Stay	2.69	4.00	< 0.001	3.56	3.6	0.36

Rastogi et al JAMA Internal Med Dec 2020

28

Inpatient Hypertension Treatment

- Worse outcomes with treatment of IP HTN
 - held true for IV and PO
- Also analyzed outcomes by severity of HTN treated
 - 140-159 and 160-199 had worse outcomes.
 - SBP >200 estimates showing harm but wide CI
- **No benefit seen no matter the route of administration or severity of HTN**

Rastogi et al JAMA Internal Med Dec 2020

29

Inpatient Hypertension treatment

- 1645 pts (9.2%) were discharged with intensified regimens.
 - In 30 days post discharge...
 - No difference in Stroke or MI
 - In 1 year...
 - No difference in Blood Pressure Control

Rastogi et al JAMA Internal Med Dec 2020

30

Inpatient Hypertension treatment

- Caveats
 - Non cardiac admissions
 - patients treated for HTN were clearly sicker... bias by indication
 - Retrospective so despite good attempt its hard to draw causality
- Take Aways
 - Treatment of acute IP HTN is unlikely to benefit and may cause harm
 - Intensifying HTN regimen on discharge not helpful

Confirm/Change my practice of not treating **asymptomatic** HTN in the hospital and not routinely intensifying regimens on discharge

Rastogi et al JAMA Internal Med Dec 2020

31

Inpatient

65 yo F w HTN, CKD, ID
Done well on IV antibio
AM.

You receive a page: Her

Hypertensive between
Amlodipine.



treatment

admitted with cellulitis.
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- Order 25 mg PO Hydralazine prn SBP >160
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32

Post-operative Bridging of Warfarin

Our patient returns... 65 yo F w HTN, CKD, DM II, and Hx of mechanical MV...

She was started on new BP meds and fell. FTH a right femoral neck fracture. She underwent ORIF with IM nail and is POD 0.

- Do you start a Heparin gtt and bridge warfarin to INR >2.5
- Start warfarin POD 0, no bridge
- Start Tx Enoxaparin as a bridge to warfarin INR >2.5
- Start a DOAC because warfarin shouldn't be given to humans

33

Post-operative Bridging of Warfarin

- RCT of Dalteparin vs Placebo for post operative bridging for patients with A-fib or Mechanical heart valves
 - n=1471, 1^o outcome: Major Thromboembolism
 - Safety Outcome: Major bleeding
 - 90 day follow up
- All patients were bridged pre-procedure
- Excluded
 - Active bleeding
 - Spinal or neurosurgery
 - CrCl <30
 - Valve with a hx of stroke or TIA
 - Multiple Mechanical Valves
 - Platelet count of <100

Kovacs et al BMJ June 2021

34

Post-operative Bridging of Warfarin

- Of 1471 patients
 - 1166 (79.3%) Afib only
 - Mean CHADs2 of 2.4
 - Mitral 133 (9.0%), Aortic Valve 172(11.7%)
- Warfarin started on POD 0 for all patients
 - Dalteparin arm bridged until Warfarin Tx
 - Ppx dose (5000 IU Dalteparin) for high bleeding risk
 - Full Tx (200 IU/kg) for low bleeding risk

Kovacs et al BMJ June 2021

35

Post-operative Bridging of Warfarin

90 days	No Bridging n=650		P value	(A-fib)		P value	(Valve)		P value
		Bridging n=820		No Bridging n=496	Bridging n=670		No Bridging n=154	Bridging n=150	
Major Thromboembolism	8 (1.2)	8 (1.0)	0.64	8 (1.6)	7 (1.0)	0.39	0	1 (0.7)	0.7
Major Bleeding	13 (2.0)	11 (1.3)	0.32	10 (2.0)	10 (1.5)	0.49	3 (1.3)	1 (0.7)	0.62
Non Major Bleeding	25 (3.9)	50 (6.1)	0.05	20 (4.0)	42 (6.3)	0.09	5 (3.3)	8 (5.3)	0.37

- No difference at 90 days in
 - Major Thromboembolism
 - Major Bleeding
- Higher rate of Non-Major Bleeding in Bridging arm

Kovacs et al BMJ June 2021

36

Post-operative Bridging of Warfarin

- Reviewer requested secondary analysis at 30 days

30 Days	No Bridging n=650	Bridging n=820	P value	Risk dif (95% CI)
Major Thromboembolism	8 (1.2)	3 (0.4)	0.06	-0.9 (-1.8 to 0.1)
Major Thromboembolism/Bleeding	16 (2.5)	12 (1.5)	0.16	-1.0 (-2.5 to 0.5)
Major Thromboembolism/ Bleeding/Death	16 (2.5)	13 (1.6)	0.23	-0.9 (-2.3 to 0.6)

- *Near statistically significant benefit for bridging*

Kovacs et al BMJ June 2021

37

Post-operative Bridging of Warfarin

- Caveats
 - Only ~5% of Patients with CHADS2 of 5-6
 - Smaller number of valve patients with important exclusions
 - Recruited for 9 years
 - Maybe some benefit early?? but why the washout
- Take Aways
 - Adds to body of recent literature showing little benefit for bridging
 - Questions still exist for High Risk AF and Mechanical Valves

Inform/confirm my practice of avoiding bridging in AF and consider not Bridging vs ppx in high risk patients with MV

Kovacs et al BMJ June 2021

38

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She was started on new BP meds and fell. FTH a right femoral neck fracture. She underwent ORIF with IM nail and is POD 0.

- a) Do you start a Heparin gtt and bridge warfarin to INR >2.5
- b) Start warfarin POD 0, no bridge **and consider ppx enox**
- c) Start Tx Enox as a bridge to warfarin and INR >2.5
- d) Start a DOAC because warfarin shouldn't be given to humans

Kovacs et al BMJ June 2021

39

What next? A-fib

65 yo F w HTN, CKD, DM II, and Hx of mechanical MV repair is now POD 2 from ORIF

You are called to bedside because of new HR 120-130, tele shows A-fib confirmed on EKG. HD stable, asymptomatic

- a) Start PO Metoprolol Tartrate and aim for rate <110
- b) Consult cardiology for consideration of cardioversion vs ablation
- c) Start Digoxin because warfarin and Dig have a nice 1980's feel
- d) Start Amiodarone load followed by a standard daily dose.

40

Rate vs Rhythm: The Never-ending Story

- RCT of early rhythm control vs usual care in early A-fib (<1 yr since dx)
 - n=2789
 - 1^o Composite Outcome: Death (CV,CVA), Hospitalization for CHF or ACS
 - Median 5.1 year follow up

Kirchof et al NEJM Oct 2020

41

Rate vs Rhythm: The Never-ending Story

- Higher risk population
 - >75 yo or had past TIA/CVA
 - Or atleast 2 of:
 - >65 yo, Female, CHF, HTN, DM, CAD, CKD III or greater, and LVH
- A-fib Characteristics
 - First episode: 38%
 - Paroxysmal: 36%
 - Persistent: 26%
 - Mean time since A-fib diagnosis: 36 days
 - CHADS2-Vasc: mean of 3.5

Kirchof et al NEJM Oct 2020

42

Rate vs Rhythm: The Never-ending Story

	Early Rhythm Control	Usual Care	Effect (95% CI)	P value
Primary Outcome	249/6399 (3.9)	316/6332 (5.0)	0.79 (0.66-0.94)	0.005
Nights in Hospital	5.8 +/- 21.9	5.1 +/- 15.5	1.08 (0.92 to 1.28)	0.23

- ~20 % RR reduction in Death (CV/stroke) or Hospitalization (CHF/ACS)
- No increase in nights in hospital

Kirchof et al NEJM Oct 2020

43

Rate vs Rhythm: The Never-ending Story

Early Rhythm Control

- Ablation: 8.0% initial, 19.4% Ablation at 2 years
- Antiarrhythmic
 - Flecainide (35.9%)
 - Amiodarone (19.6%)
 - Dronedarone (16.7%)
 - 35% off rhythm control at 2yrs

Usual Care

- Antiarrhythmic use
 - 2.0% initial, 7.6% at 2 years
- Ablation
 - 7.0% at 2 years

~90% on anticoagulation at year 2 in both arms

Kirchof et al NEJM Oct 2020

44

What next? A-fib

- **Caveats**
 - Fairly sick/high risk patients with Afib -> high risk of complication from rhythm
 - All patients continued to receive AC and rate control
- **Take Aways**
 - Majority of patients tolerated rhythm control
 - In New/Early onset Afib Rhythm control is likely better (particularly ablation)
- **Change my practice** to refer new/early Afib to Electrophysiology and avoid antiarrhythmic agents less in addition to AC and Rate control.

Kirchof et al NEJM Oct 2020

45

What next? A-fib

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You are called to bedside because of new HR 120-130, tele shows A-fib confirmed on EKG. HD stable, asymptomatic

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46

Diabetes Management

Our patient: 65 yo F w HTN, CKD, DM II, and Hx of mechanical MV repair s/p ORIF is finally nearing discharge.

You review her meds and data and notice that she has been fairly Hyperglycemic to 200's and regularly receiving sliding scale insulin. Home Metformin has been held.

- a) Start a new low dose of Long Acting insulin on discharge
- b) Add an SGLT-2i because it seems to help with everything
- c) Add a Sulfonylurea to her home Metformin
- d) Pretend you never saw anything and press the discharge button

47

Diabetes Management on DC

- Retrospective Cohort and Propensity Matching of Hospitalized Patients with Diabetes not on insulin
 - Large VA study
 - 28,198 pts, 115 hospitals
 - 98% male, ~80% white
 - Primary Exposure: New or intensified DM regimen
 - 2768 pts, 9.8%
 - 1423 insulins (51.4) or 640 sulfonylureas (23.1%)

Anderson et al JAMA Open Oct 2021

48

Diabetes Management on DC

- Propensity Matched Analysis
 - 30 and 365 day outcomes

@ 30 days	Intensified Regimen n=2648	No Intensified Regimen n=2648	HR (95% CI)
Severe Hypoglycemia	26 (1.0)	12 (0.5)	2.17 (1.10-4.28)
Severe Hyperglycemia	7 (0.3)	7 (0.3)	1.00 (0.33-3.08)
Mortality	35 (1.3)	63 (2.4)	0.55 (0.33-0.92)
Readmission	457 (17.3)	433 (16.4)	1.06 (0.93-1.20)

Anderson et al JAMA Open Oct 2021

49

Diabetes Management on DC

- All differences disappeared at 1 year of follow up
- Secondary Analysis of disease control
 - No change in mean Hgb A1c at 1 year
- Analysis stratified by baseline Hgb A1c
 - No difference in severe hypo or hyperglycemia

Anderson et al JAMA Open Oct 2021

50

Diabetes Management on DC

- Caveats
 - Retrospective with clear bias by indication
 - VA study so limited ability to generalize
- Take Aways
 - Intensification of DM regimen in patients not taking insulin increases the risk for post discharge hypoglycemia without reducing severe hyperglycemia

Confirm my practice of resuming patients home DM discharge regimens unless there is a clear acute indication for change

Anderson et al JAMA Open Oct 2021

51

Diabetes Management

Our patient: 65 yo F w
repair s/p ORIF is final

You review her meds and
Hyperglycemic to 200's
Home Metformin has b



mechanical MV

has been fairly
dosing scale insulin.

- Start a new low dose of Long Acting insulin on discharge
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52

In Summary

- SGLT-2 has clear benefit in HFrEF, HFpEF*, CKD, and oh DM too
- IV Iron for Iron Deficiency Post HF exacerbation decreases risk of HF hospitalization
- Discharge before noon is not going to save us
- Restrictive Transfusion Protocol (Hgb<8) was non-inferior in patients with an active myocardial ischemia

53

In Summary

- Rate vs Rhythm control debate in A-fib is not dead, see an electrophysiologist
- Bridging warfarin post operatively likely has limited if any benefit in Afib and potentially in mechanical valves as well
- No benefit seen in treating asymptomatic inpatient Hypertension and may causes harm
- Intensifying discharge regimens for HTN and DM is unlikely to be helpful

54

References

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Thank You

56