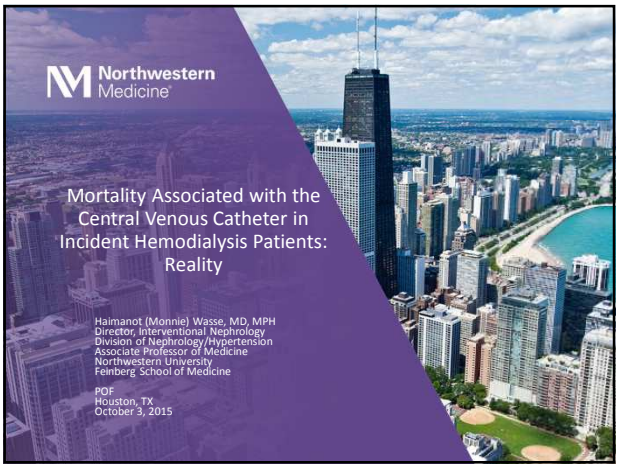


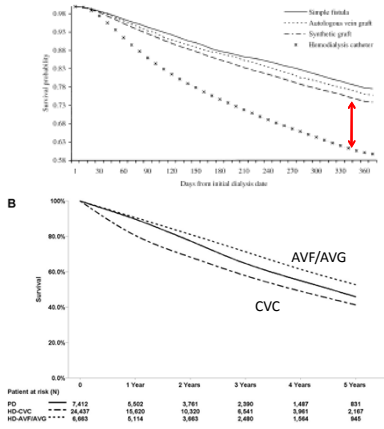
Disclosures

- Employer: Northwestern University
- Consultant: Humacyte, Cryolife, Proteon

What does existing data demonstrate?

Cohort studies, registry data consistently link CVC use with increased mortality in incident HD patients

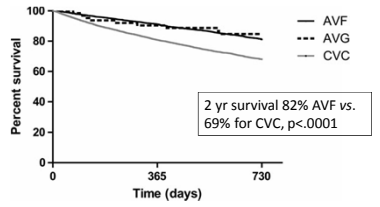
- Xue J et al, AJKD, 2003
  - Cohort of Incident U.S. patients > 67 yo., CVC use associated with 2-fold greater risk of death in first 90 days of dialysis
- Pisoni RI et al, AJKD, 2009
  - DOPPS, CVC use confers ~40% greater mortality risk among US patients
- Lukowsky LR et al, Am J Neph, 2012
  - CVC use explains 34% of deaths in first 90 days among 18K incident patients
- Chan et al, CJASN, 2011
  - Initiating dalysis with an AVF decreased early death risk by 61% vs CVC use in first 2 weeks of dialysis (n=303K Fresenius patients)



Xue et al, AJKD

Perl J et al, JASN,2011. 20% greater mortality in CVC users at year 5.
Adjusted for age, race, gender, comorbidity index, serum albumin, late referral, eGFR, province of treatment

2-year survival by vascular access type



- ERA-EDTA Registry, ~11K incident patients, 15 countries
- Increased use of CVC, declining AVF at dialysis start
- **After adjustment, all-cause mortality in those in incident AVF users was 43% lower than CVC users**

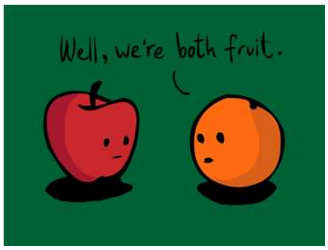
Ravani P et al, NDT, 2014

Primary Mechanisms of Mortality

- 500K patients, 193K death over 5 year follow up
  - CV-related mortality 38% lower among patients with an AVF
- Catheter-related bacteremia
  - 0.55 events/1000 catheter days elderly
  - 1.28- 1.97 events/1000 catheter days non-elderly
    - Consider differences in rates of bacterial conolonization of nares, skin

Murea M et al, CJASN 2014; Beathard et al, Sem Dial, 2003

Are we examining two different patient populations?



Limitation of observational studies to date

- Patients using a CVC differ from those with permanent AV access:
  - Older
  - Greater co-morbidity burden
  - Lower serum albumin

All factors associated with a greater risk of mortality

Is there selection bias?

Key Question

- Is excess mortality in CVC-users due to the CVC or is it a marker of patients more likely to die?
  - Does change from AV access to CVC increase risk of death?
  - Does change from a CVC to AV access reduce risk of death?

- HEMO Study (Allon et al)
  - Multicenter RCT examining effect of dialysis dose/flux on morbidity and mortality of HD patients
    - 15 clinical centers, 72 dialysis units
    - Incident ESRD, 1,826 pts, follow-up ~2.8 years
    - Recorded monthly access (CVC vs permanent)
  - Examined:
    - Mortality risk at each time point related to patient's current access type
    - Mortality risk following 1-yr after randomization to change in access type from 1 year earlier

Allon M et al, AJKD, 2006

- Baseline:
  - Risk of mortality 3-fold greater in patients using a CVC vs permanent access
    - 62% greater risk of cardiac death
    - 2.3-fold greater risk of infection-related death
- Change from permanent access to CVC: 2-fold **greater** risk of death compared to patients using permanent access at both times
- Change from catheter to AV access **reduced** risk of death compared with CVC use at both times

Allon M et al, AJKD, 2006

- Change from an AV access to catheter:
  - Decline in albumin, weight loss, PCR, increased hospitalization
- Change from a catheter to AV access after 6 months:
  - Reduced hospitalization

Allon M et al, AJKD, 2006

- Authors conclusion:
  - Catheter use is an independent predictor of patient mortality
    - Does not prove causality, but does reduce risk for confounding from patient characteristics
    - Suggests that the CVC contributes to excess mortality in ESRD patients

Allon M et al, AJKD, 2006

Converting to permanent AV access reduces mortality

- DOPPS U.S. incident ESRD patient cohort (n= ~4500)
  - CVC to AV access: 31% **lower** risk of death
    - Effect similar for AVF or AVG
    - Persisted across demographic groups/facility with different conversion practices
  - AV access to CVC: 81% **greater** risk of death

Bradbury BD et al, AJKD 2009

Slow Transition Time to Permanent AV Access

- ~60% of incident ESRD patients initially using CVC fail to transition by 90 days
  - Patients >75yo *vs*. < 50 yo were 2-fold more likely to remain CVC dependent at 90 days
- Mortality 23% lower in patients initiating with an AVF vs those with an AVF awaiting maturation of an AVF (p<.001)

Wasse H et al, AJKD, 2006, Males M et al, Arch Surg, 2015

Additional factors driving incident CVC use

- CVC-related mortality isn't just due to greater a greater burden of comorbid conditions
- 65% of patients referred for access creation ~1 yr prior to dialysis initiation initiate with a CVC
  - Missed access-related appointments

Avorn et al, AJKD 2001; Astor B AJKD, 2001; Lee T AJKD, 2004

Conclusions

- CVC use and mortality strongly associated, yet:
  - Observational studies are imperfect
  - Selection bias is present; accounting for it reduces strength of association
- Should this lead us to consider CVC's = AVF? No
  - CVC's increase risk of cardiovascular, infection-related death, central venous stenosis/occlusion, associate with subsequent AV access dysfunction
- Consistent evidence shows that incident HD patients reduce their risk of death when converting from a CVC to AV access

Will we ever know with absolute certainty?

Conclusions

- Perfect world we'd do RCT to compare mortality of patients by vascular access type
- **More important question**:
  - **How do we reduce the number of incident HD patients using a CVC?**
    - Improve surgical resources, train dedicated clinicians, increase use of preoperative diagnostic imaging

S Van der Veer et al, JVA, 2014