Brain Death

Turning Tragedy into Opportunities

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Introduction

- Conflicts of Interest: None

- Goals:
  - Review the role of Legacy of Hope with process of organ donation
    - Show needs
    - Show how answering needs
  - Demystify the brain death process
    - Unique physiology
    - Brain death declaration
    - Steps to make declaration smoother process
  - Extend the gifts each donor has to give
    - ↑ Organs per donor
    - Grief processing and closure for families

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Introduction

- Outline
  - Background
  - The Need and the Answer to the Need
  - Identifying the Patient and the Potential
  - Physiology of the Brain Death Process
  - Brain Death Declaration
  - Organ Donor Management and Successes

Background

- Trauma Surgeon 2000 - current
  - Anywhere from 3-7 call nights per month
    - 10 – 25 admits
    - 50 curse words / night; 1-2 punches at team by pt
    - Little “thanks”
- Surgical Intensivist 2004-current
  - Director of 20 bed ICU
  - Work on “one” to get “one” better
  - Receive “thanks”

Background

- AOC (Legacy of Hope)
  - Approached in February 2015
  - Describe their plans for Organ Recovery Center
    - 2 ICU Beds
    - 2 OR suites
    - Bring donors from around the state
  - Goals:
    - Increase organs per donor
    - Improve SRTR
    - Develop protocols to optimize donor management

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Background

- Before LoH Recovery center
  - Drove to hospitals with coordinators
    - Broad range of capabilities at various sites
    - Various “buy-in” from physicians and teams
    - Impressed with the coordinators and abilities to adapt
  - Learned management on site
  - Some literature out there on management

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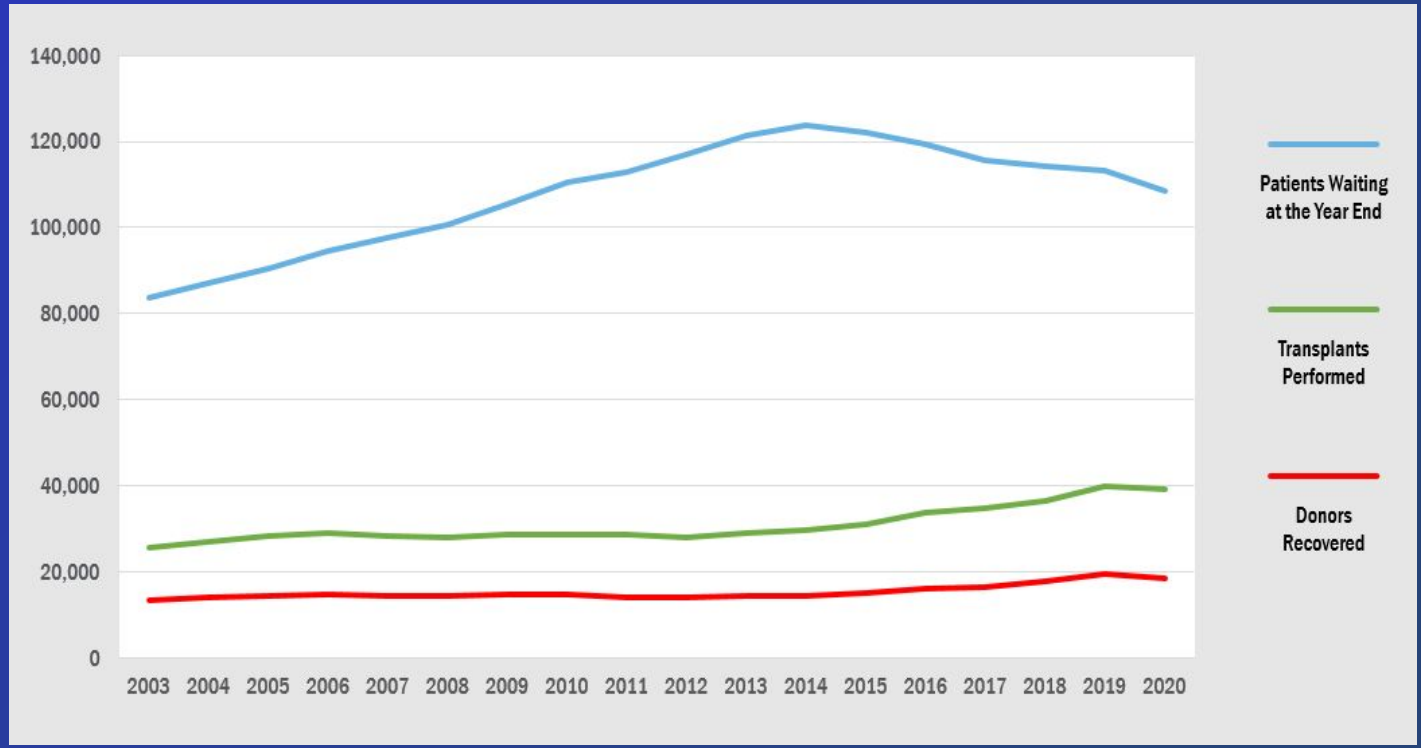
Background

- LoH
  - Medical Director of LoH
    - 2 ICU beds
    - 2 OR’s
    - Select ICU RN
    - Coordinators
    - Families!
    - 1 life 6-7 lives

The Need and Answer to the Need

- Challenges Faced:
  - 2.2 mil people die/yr in US
    - < 1% die in manner to allow organ donation
  - 110-115k waiting list
  - 100 added each day
  - 15-20 die each day



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The Need and Answer to the Need

- Final Rule
  - All OPO will be graded on 2 metrics:
    - Donation rate—number patients donating / inpatient deaths
    - Transplant rate—number organs transplanted / total donors

    - Potential challenges calculating each number
    - If fall below certain thresholds, can lose your OPO coverage area! We need all the help we can get!
      - EVERY ONE OF YOU CAN MAKE A DIFFERENCE IN AT LEAST ONE STEP IN THIS PROCESS

The Need and Answer to the Need

- Steps to Close the Gap
  - Living Related Organ Donation—Locke
  - Xenotransplant
  - Organ 3-D building/ stem cell therapy
  - Donation after cardiac death
    - Challenges faced:
      - Declaring physician
  - Brain Dead Organ Donation

The Need and the Answer to the Need

- Brain Dead Organ Donation
  - Increase the registered donors
  - Increase the referrals
  - Increase family consent to donation
  - Preserve the chance for donation in potential donors
  - Optimize donor management

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Identifying the Patient and the Potential

- Brain dead organ donation
  - Increase the referral
    - Timely referral
      - 1998 CMS timely referral rule
        - Notify OPO within 1 hour of 3 findings:
          - No pupil response
          - No cough
          - No gag
          - No response to pain
          - No spontaneous breaths
        - Or change to withdrawal for the goals of care
    - UAB / LoH has created a Cerner notification system

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Identifying the Patient and the Potential

- Brain dead organ donation
  - Increase the family consent to donation
    - Designated requestor
    - Separate “bad news” from “approach”
      - Team can’t care for the patient and then ask for organs—public concern for “they just wanted his/her organs”
      - Important in the grief process
    - Family witnessing and understanding the brain death exam
    - The Organ Alliance—key words
    - LoH SIM Course with UAB OIPS: brain death exam & family communication

Identifying the Patient and the Potential

- Brain dead organ donor
  - Preserve the chance for donation in potential donors
    - GOOD CARE
      - Brain death process is only one type of “injury” to organs
      - Sometimes harder to overcome a decrease in level of care
        - Turning, suctioning, “routine” care
        - “Non-survivable” so….
        - High UOP
        - Hypotension

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Identifying the Patient and the Potential

- Brain dead organ donor
  - Preserve the chance for donation in potential organ donor
    - Catastrophic Brain Injury Guidelines
      - Maintain SBP > 90
        - Consider invasive monitoring and access
        - Vasopressor support
      - Maintain UOP: 0.5—1cc/kg/hr and < 300cc/hr
        - Fluid if behind
        - Vasopressin if DI
      - Maintain PaO2 > 100
      - Maintain pH 7.35 – 7.45

Identifying the Patient and the Potential

- Brain dead organ donor
  - Preserve the chance for donation in potential donors
    - CBIGs
      - Crit Care Med 2012 :
        - Adopt DMG 3.6 organs /donor >4 organs per donor
          - Would mean 70-80 more organs transplanted in state of Alabama with our last year referrals
      - JAMA Surg 2014:
        - DMG for ECD 2.1 organs/donor 3 organs /donor
          - Would mean 150-180 more organs in state of Alabama

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Identifying the Patient and the Potential

- Brain dead organ donor
  - Optimize donor management
    - PTC and myself
    - Successes

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Physiology of Brain Death Process

- Physiology and Pathophysiology
  - What happens as patient progresses to brain death
  - Defined in 90's, South Africa, animal models
    - EKG, PA cath, histology, hemodynamics, chemistries, etc
  - Brain death processes
    - Inflammatory changes
    - Circulatory changes (autonomic storm)
    - Metabolic changes
    - Hormonal changes

Physiology of Brain Death Process

- Physiology and Pathophysiology
  - Inflammatory
    - Cytokines, Interleukins, inflammatory pathways
    - TNF, IL-6, IL-8, IL-10, IFN-γ
      - Vasodilation
      - Third spacing
      - Coagulopathy
      - Decrease organ function (donor & recipient)
    - Blood brain barrier disruption (GSW head)
      - Release tissue factor
      - Bleed DIC

Schwarz, Cell Transplantation, 2018

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Physiology of Brain Death Process

- Physiology and Pathophysiology
  - Circulatory Changes
    - Early changes: ↑ SVR and MAP
    - Pre-herniation: fluid shifts to capacitance vessels and lungs
    - Herniation:
      - ↑↑ SVR
      - ↓ C.O.
      - MV regurg □ ↑ LA pressure □ ↑↑ pulm edema
    - Post-herniation: circulatory collapse following catechol surg from cardiac dysfunction and catechol depletion

Physiology of Brain Death Process

- Physiology and Pathophysiology
  - Histology/Organ changes
    - Heart fibers damage as result of catechol surge and calcium shifts
      - Contraction band necrosis
      - Mononuclear infiltrate
    - Lungs develop significant edema
    - Kidneys develop ATN
      - Hypoperfusion
      - Energetics
      - Worsened with hypovolemia due to DI

Physiology of Brain Death Process

- Physiology and Pathophysiology
  - Metabolic changes
    - Hypothermia
    - Acidosis
      - Renal dysfunction
      - Hyperchloridemia
    - Hypocalcemia
    - Hypophosphatemia

Physiology of Brain Death Process

- Physiology and Pathophysiology
  - Hormonal changes—whole separate lecture but focus on what you see
    - No perfusion of brain results in no hormones output from hypothalamus/pituitary
    - So all hormones will disappear over time, depending of half life

Physiology of Brain Death Process

- Physiology and Pathophysiology
  - Hormonal changes
    - Vasopressin
      - Acts on 3 different receptors in the body
        - Vasomotor tone, platelets, uterine
        - Anterior pituitary
        - Renal receptor
      - Half life 10 – 35 min
      - Why UOP often picks up at brain death
      - Start infusion early, helps stability and prevent DI
      - I recommend use during apnea test

Physiology of Brain Death Process

- Physiology and Pathophysiology
  - Hormonal changes
    - Thyroid
      - Disappearance complex—different forms and interactions
      - Usually start drip in order to stabilize hemodynamics and restore cellular energetics
      - Thyroid replacement usually increases ability to transplant heart and lungs

Physiology of Brain Death Process

- Physiology and Pathophysiology
  - Hormonal
    - Stress Hormones: Glucocorticoid/Mineralocorticoid
      - Half life of ACTH 10 min, so within hour of brain death, level low to none
      - Steroids replacement in donor management: helps with adrenal insufficiency and inflammatory changes of brain death
      - In general 1gm load then 1mg/kg BID
      - Addition of steroids probably associated with organ improvement

Brain Death Declaration

- Various Injuries
  - Overdose
  - Trauma
  - Hypoxia
  - Cardiac arrest
- Common Result: complete and irreversible cessation of brain function
  - Cerebrum only—coma
  - Brainstem only—locked in syndrome

Brain Death Declaration

- Brain death declaration
  - AL: 2 physicians required
  - Cause of brain death must be known
    - If unknown further testing should be undertaken
    - If unknown, prudent to allow 6-12 hours between exams
  - No confounding meds
    - Testing for levels of meds in system—pitfall UDS
    - 3.5 – 5 half lives for medication clearance or reverse med
  - Temp— > 36.5
  - SBP adequate— > 100mmHg

Brain Death Declaration

- Brain death declaration
  - Family present helps—having family present has been shown to increase the consent rate
    - Improves understanding and acceptance
    - Allows them ability to visualize absence of function
    - Talk them thru the testing
      - Educate about spinal reflexes
      - Explain the steps of the exam

Brain Death Declaration

- Brain death declaration
  - Corneal: no blink in response to stimuli
  - Pupil: no constriction with light
  - Doll's Eye: brain death, eyes move with nose. Non-brain dead, the eyes move opposite of direction of head turn/stay fixed on ceiling

  - Gag: No gag with pharyngeal stimulation
  - Cough: No cough with deep suctioning

Brain Death Declaration

- Brain death declaration
  - Occulovestibular—there is no fast-twitch eye movement with temp stimulation of vestibule
    - 50cc in each ear
    - Head of bed 30 degrees
    - COWS
    - Watch for response up to 1 minute per ear

Brain Death Declaration

- Brain death declaration
  - Apnea:
    - Disconnect from vent; tubing with O2 flowing into ETT
    - Serial ABG to eval for increase in CO2 by 20
      (CO2 ↑ 4mmHg for every 1 minute—in most)
    - Absence of any attempt for breath

    - Keys:
      - Hemodynamic support in place/avail
      - If hypovolemia, 500-1000cc prior to exam
      - Pre-oxygenate 5-10 min
      - Tube size / Flow rate of O_2

Organ Donor Management and Successes

- Vision to build recovery center started to develop in 2014/2015
  - 58 OPO's
    - ~5 had recovery centers
    - No recovery centers attached to hospital
  - Joined in 2015
    - Develop protocols for management in the recovery center
    - Improved organs / donor
    - Improved Observed to Expected metric for each organ
      - Lungs SRTR 0.3 – 0.4
      - Heart SRTR 0.7 – 0.8
      - Liver SRTR > 1
      - Kidney SRTR 0.85 – 0.92
      - Pancreas SRTR 0.7

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Organ Donor Management and Successes

- Completed early 2016
- Immediately saw benefits of attached donor recovery center
  - Allowed closer following of donors
  - Allowed direct interaction between PTC and intensivist
  - Allowed real time teaching for management and development of protocols
  - Faster time to complete procedures needed for each donor
  - Select group of bedside ICU nurses that had interest in transplantation

Organ Donor Management and Successes

- Pulmonary
  - 2016 began the creation of the pulmonary protocol
  - Started here as this was lowest yield organ for our OPO
  - Protocol Keys:
    - Work for variety of problems:

Atelectasis	Plugging	Edema
Inflammation	Pulmonary contusions	Pneumonia
Reactive airways		

    - Simple
    - Had to work in different settings, ventilators, varying support

Organ Donor Management and Successes

- Pulmonary
  - Data needed at start

Height:_____cm	Weight:_____kg	BMI:_____
In:_____cc	Out:_____cc	
pH _____	MV_____	pCO2_____

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Organ Donor Management and Successes

- Pulmonary

STEPS

1. Calculate the ideal body weight in kg _____kg

   Ideal weight = (Patient weight x 25) ÷ Patient BMI

2. Tidal Volume _____cc

   Ideal body weight (Step 1) X 7cc

3. Calculate Minute Ventilatory Need _____ L/min

   Minute Ventilatory Need = (current minute ventilation x Current CO2) ÷ Desired CO2

4. Calculate Vent Rate _____

   Vent Rate = (Minute Ventilatory Need ÷ Tidal Volume) x 1000

5. Set ventilator with settings determined in # 2, #3, #4

   AC / ventilator rate / tidal volume / PEEP / FiO2

6. Slow the flow so that I:E = 1:1

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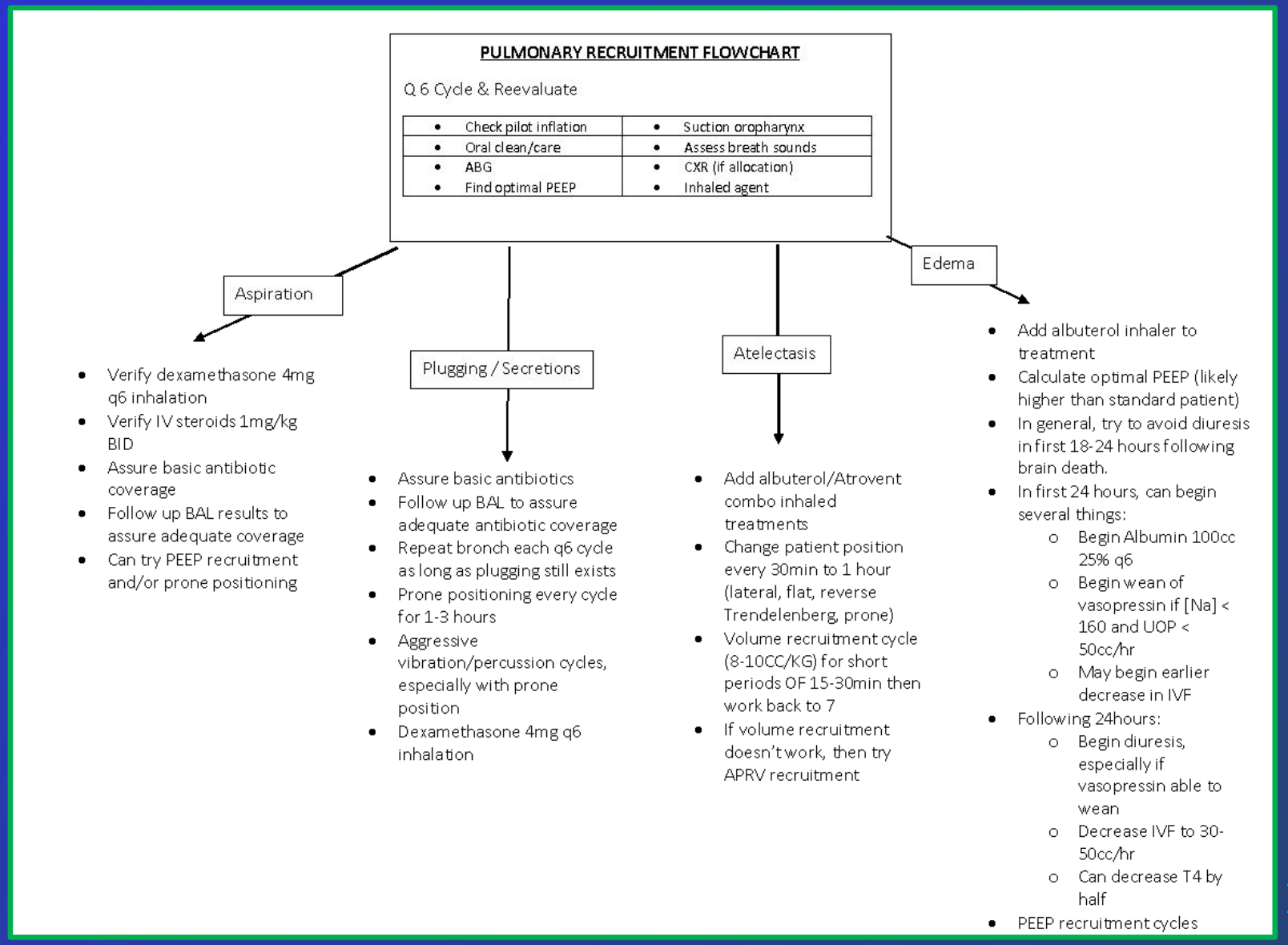
Organ Donor Management and Successes

- Pulmonary

7. Calculate Optimal PEEP
   a. Set PEEP
   b. Press Inspiratory Hold
   c. Chart static compliance
   d. Change PEEP by increments 1-2 and repeat b & c

PEEP	Compliance
5	
6	
7	
8	
9	
10	
11	
12	

Organ Donor Management and Successes



PULMONARY RECRUITMENT FLOWCHART

Q 6 Cycle & Reevaluate

• Check pilot inflation	• Suction oropharynx
• Oral clean/care	• Assess breath sounds
• ABG	• CXR (if allocation)
• Find optimal PEEP	• Inhaled agent

Aspiration

- Verify dexamethasone 4mg q6 inhalation
- Verify IV steroids 1mg/kg BID
- Assure basic antibiotic coverage
- Follow up BAL results to assure adequate coverage
- Can try PEEP recruitment and/or prone positioning

Plugging / Secretions

- Assure basic antibiotics
- Follow up BAL to assure adequate antibiotic coverage
- Repeat bronch each q6 cycle as long as plugging still exists
- Prone positioning every cycle for 1-3 hours
- Aggressive vibration/percussion cycles, especially with prone position
- Dexamethasone 4mg q6 inhalation

Atelectasis

- Add albuterol/Atrovent combo inhaled treatments
- Change patient position every 30min to 1 hour (lateral, flat, reverse Trendelenberg, prone)
- Volume recruitment cycle (8-10CC/KG) for short periods OF 15-30min then work back to 7
- If volume recruitment doesn't work, then try APRV recruitment

Edema

- Add albuterol inhaler to treatment
- Calculate optimal PEEP (likely higher than standard patient)
- In general, try to avoid diuresis in first 18-24 hours following brain death.
- In first 24 hours, can begin several things:
  - Begin Albumin 100cc 25% q6
  - Begin wean of vasopressin if [Na] < 160 and UOP < 50cc/hr
  - May begin earlier decrease in IVF
- Following 24hours:
  - Begin diuresis, especially if vasopressin able to wean
  - Decrease IVF to 30-50cc/hr
  - Can decrease T4 by half
- PEEP recruitment cycles

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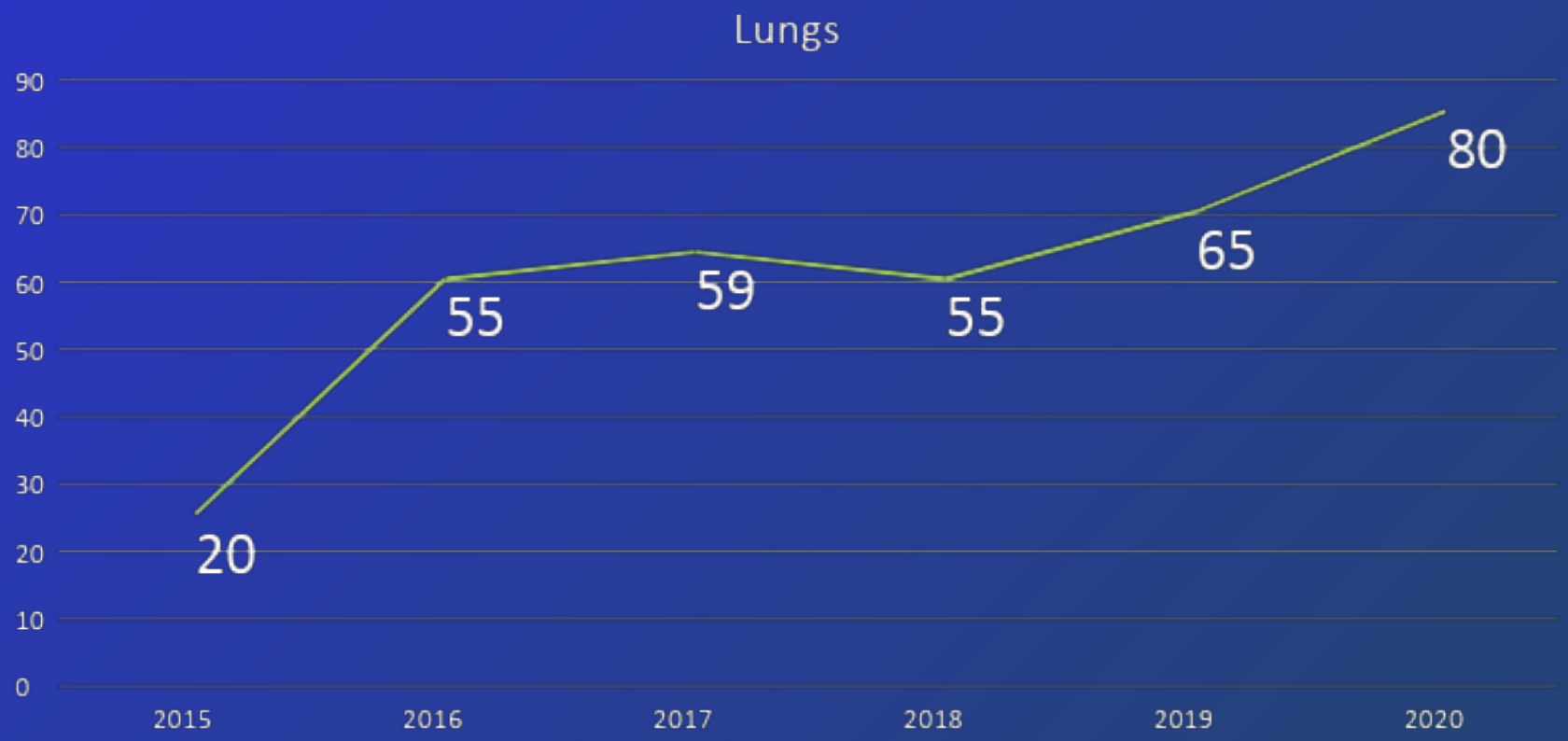
Organ Donor Management and Successes

- Pulmonary



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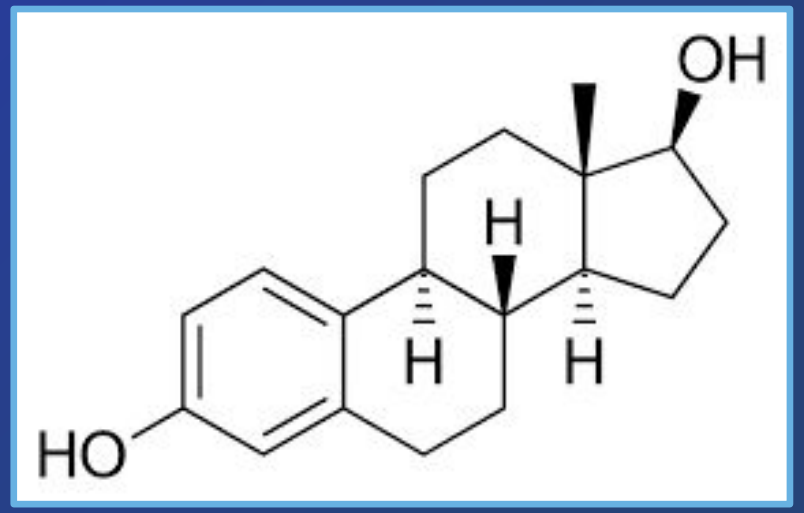
Organ Donor Management and Successes

- Cardiac
  - PTC and I pulled heart data
    - Heart Declines:
      - LVH
      - CADz
      - Other diseases (Hep C)
      - Poor EF—Neurogenic stunned myocardium
    - Neurogenic stunned myocardium
      - Chart review: young males and middle age females

Organ Donor Management and Successes

- Cardiac
  - Basic science work
    - Looking into pathology behind neurogenic stunning
    - Basic science of estrogen with Irshad Chaudry
  - 2017 began estrogen protocol
    - 32 hearts 58 hearts in one year
  - 2019: estrogen + heparin protocol
    - 77 hearts



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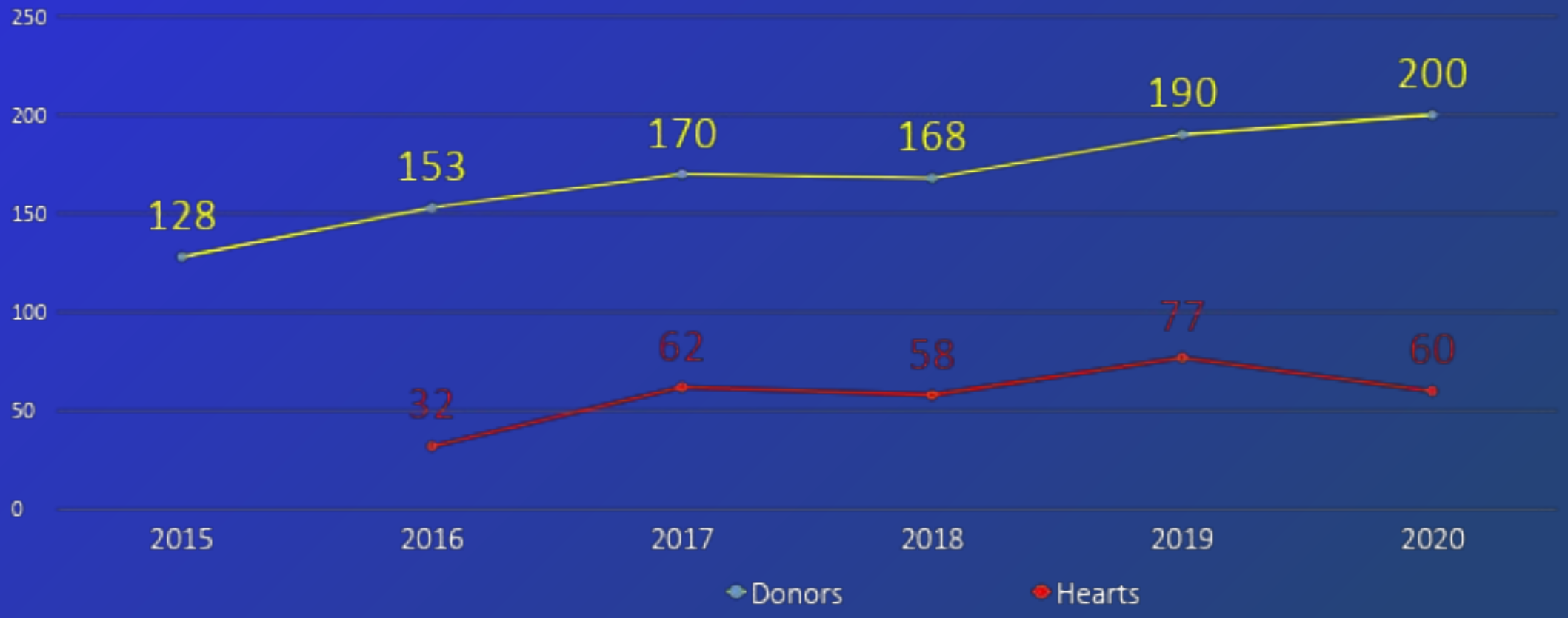
Organ Donor Management and Successes



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Organ Donor Management and Successes

- Kidneys
  - Project started in 2018
    - “Cool Beans Protocol”
      - Passive hypothermia 34-35 C
      - Low dose dopamine

      - Mid-year review of data: still underperforming as compared to other OPO
      - Reviewed renal biopsies
        - Microvascular thrombosis DIC

Organ Donor Management and Successes

- Kidneys
  - Last half of 2018:
    - Followed D-dimer, platelet, fibrinogen, INR, split products
    - Strongest correlation: platelet, D-dimer, creatinine
    - LOH Score

Lab	Range	Points
Platelet	>100k	0
	50-100K	1
	< 50K	2
D-Dimer	0-240 ng/mL	0
	240 – 2000 ng/mL	1
	> 2000 ng/mL	2
Creatinine	< 1.4 mg/dL	0
	> 1.4 mg / dL	1

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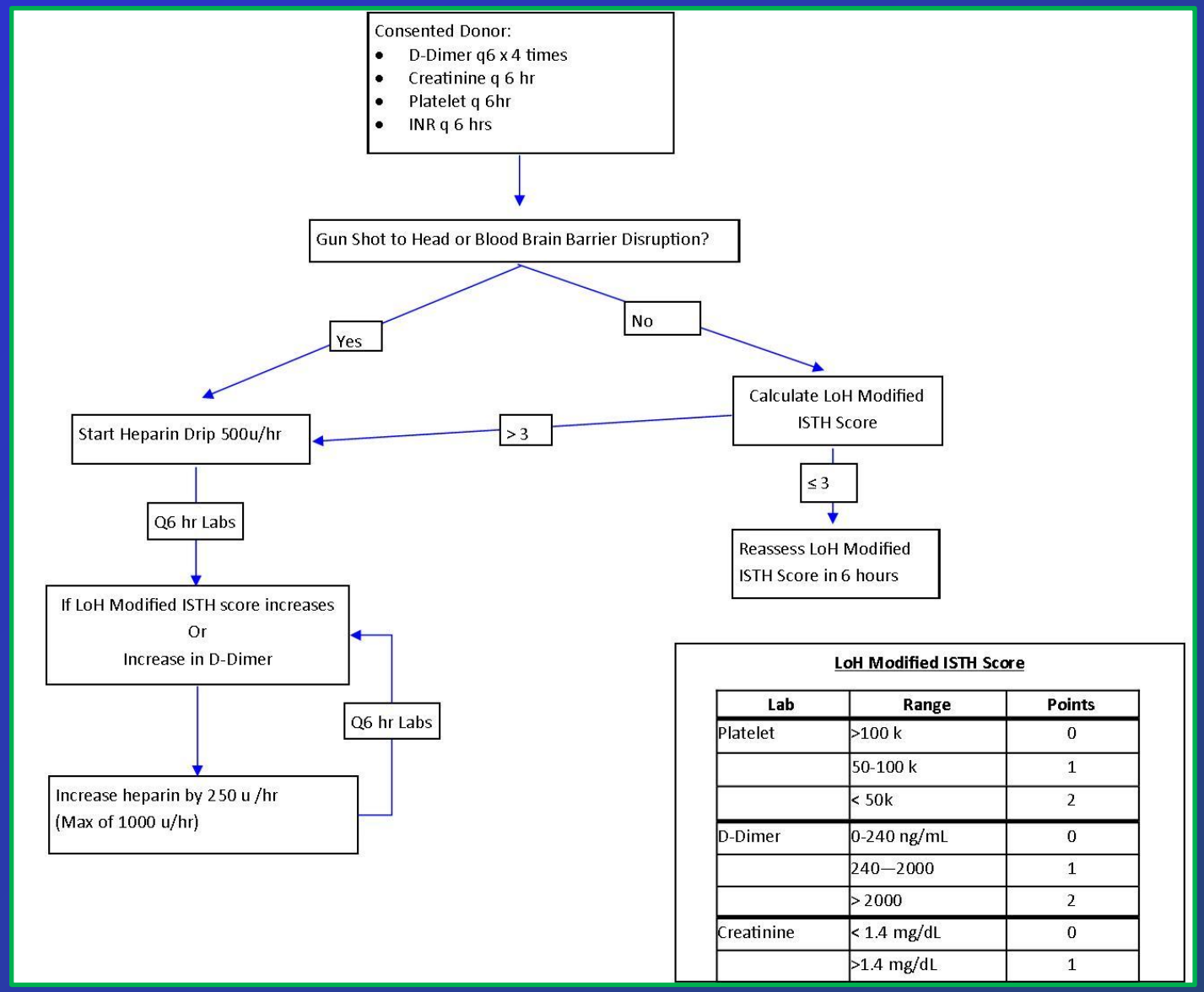
Organ Donor Management and Successes



LoH Modified ISTH Score

Lab	Range	Points
Platelet	>100 k	0
	50-100 k	1
	< 50k	2
D-Dimer	0-240 ng/mL	0
	240—2000	1
	> 2000	2
Creatinine	< 1.4 mg/dL	0
	>1.4 mg/dL	1

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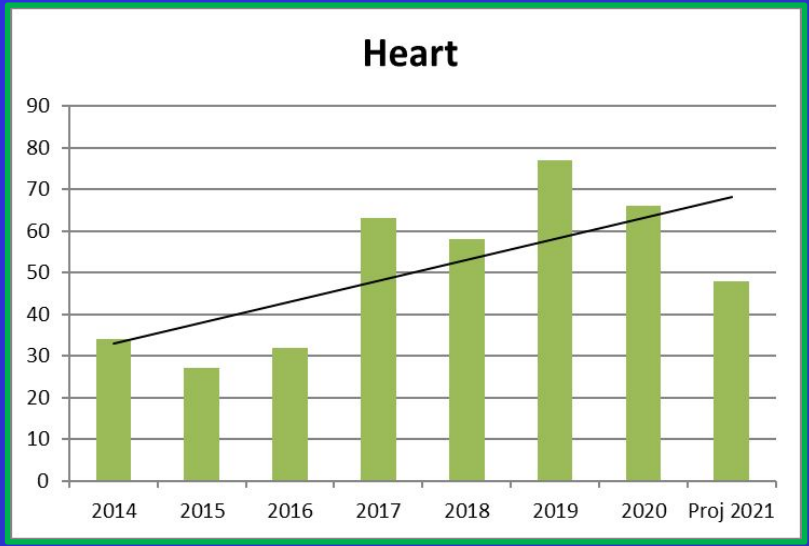
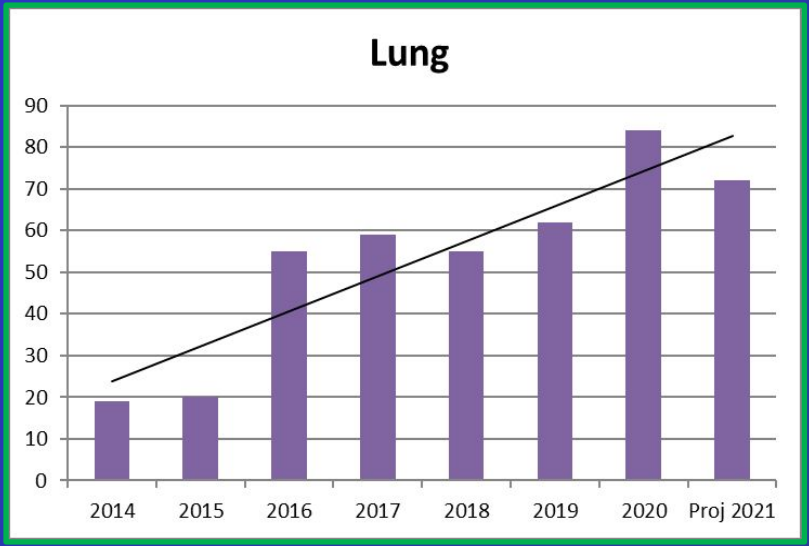
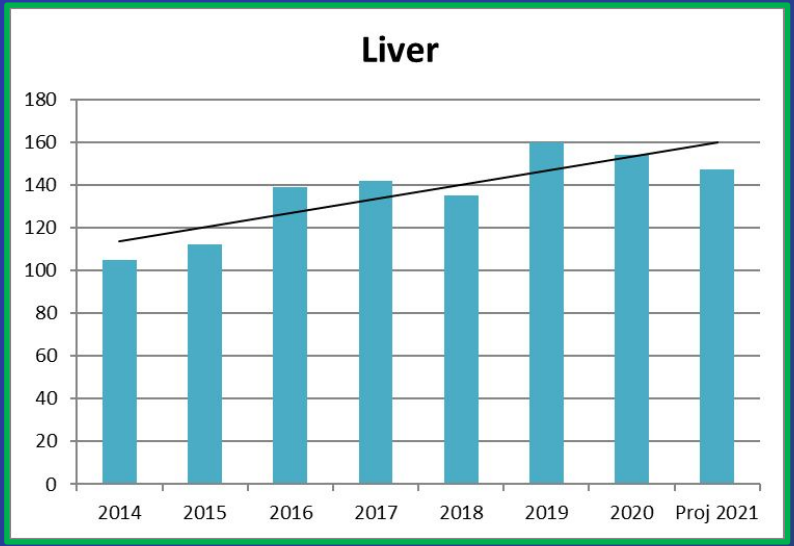
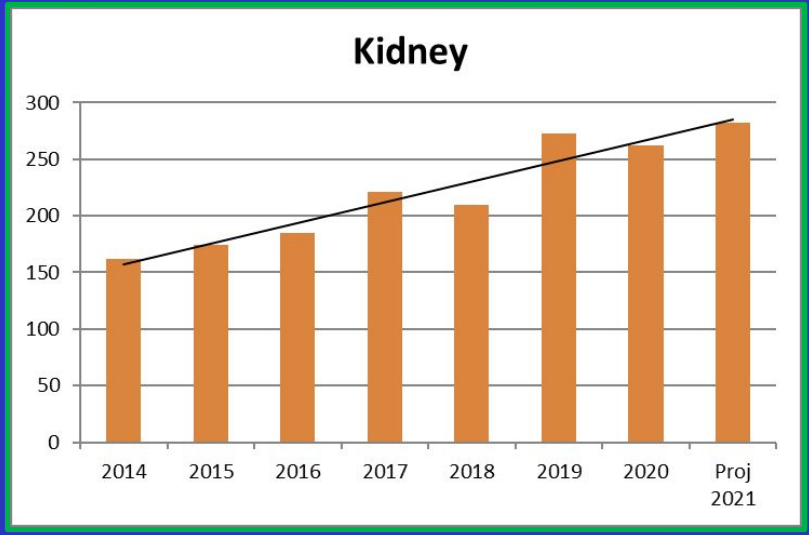
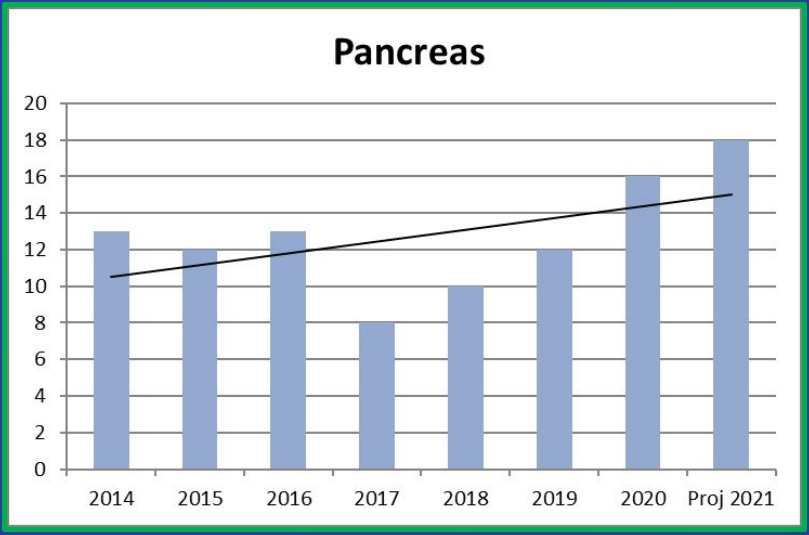
Organ Donor Management and Successes

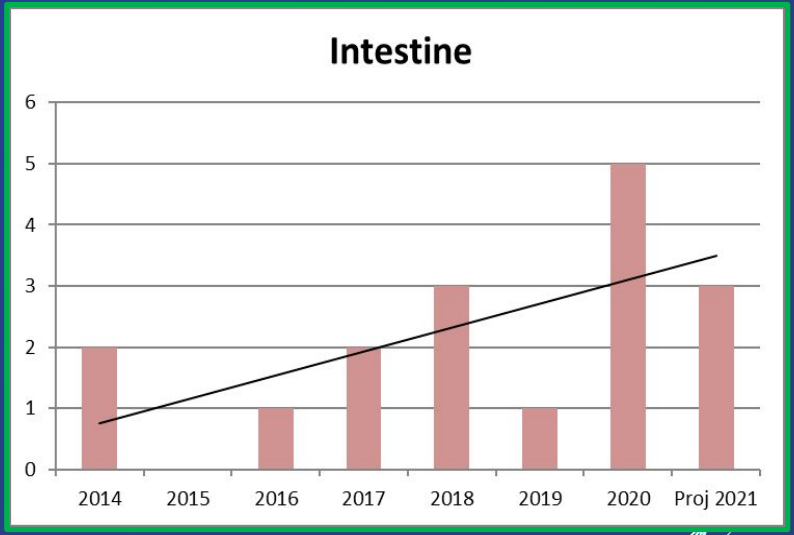












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Brain Death: Turning Tragedy into Opportunities

- The Need is Great
- So many steps can make a difference
  - Recognition of the Potential
  - Timely referral
  - Care of the patient
  - Care of the patient progressing
  - Care of the family during the process
  - Organ donor management—my team and I wouldn't have that chance if not for you

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Brain Death: Turning Tragedy into Opportunities

- Questions

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