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Stephen E. Follansbee

Director, HIV Services

Kaiser Medical Center, SF

Vaccines-1

- **Pneumococcal (P772) VAMC**
- Incidence rate ratio (IRR) HIV+/HIV-
- IRR 9.35 overall (23/604 vs 1/279; $p < 0.01$)
 - AA 4.1
 - smokers 5.3
 - binge drinkers 7.1
 - DM 1.5
 - COPD 3.8

Vaccines-2

- **Influenza (P231)**-Japanese, non-randomized
- Infection diagnosed by culture, serology, PCR
- 9.5% V (25/262) vs 25.8% non-V (17/66) (p<0.001)
- <150 CD4+ 7/26 vs 2/5 (N.S.)

Vaccine-3

- **Hepatitis A (P830) USA**
- 123 vaccinated x 2
- 61 (50% responders)
- CD4+ cells: R 486 vs NR 358
- Multivariant analysis: females and higher CD4+ predictive of response

Surgical Outcomes of HIV+ Patients in the Era of HAART

Kaiser Permanente Northern California

Michael Horberg, MD

Leo Hurley, MPH

Daniel Klein, MD

Stephen Follansbee, MD

Charles Quesenberry, PhD

Jason Flamm, MD

Gary Green, MD

Tye Luu, RN



Methods - 1

- Case patients:

HIV+ members with one or more of selected surgical procedures in the period 7/1997-6/2002 and diagnosed with HIV before surgery.

- Control patients:

HIV- members matched to HIV+ cases on:

| | |
|-----------------------------|---------------|
| Gender: | exact match |
| Age (year of birth): | best possible |
| Type of surgical procedure: | exact match |
| Year of surgery: | best possible |
| Medical center of surgery: | best possible |

Methods - 2

- Surgical procedures selected for study:
 - appendectomy
 - cholecystectomy
 - hernia repair (inguinal, umbilical, ventral)
 - colon resection
 - CABG or cardiac valve replacement
 - hip or knee replacement
 - mastectomy
 - hysterectomy (+/- oophorectomy)

Methods - 3

- Manual chart review through 1 yr post-surgery
 - confirm surgery, HIV status and membership
 - document co-morbidities and h/o OIs
 - identify complications of surgery (including wound infection, pneumonia, cardiac event, revision OR)
 - count visits to surgeon in 3 months post surgery
 - determine follow-up and vital status at 12 mo
- Lab values extracted from electronic systems
 - CD4 count, Viral load, WBC count, Hemoglobin

Methods - 4

- Analyses
 - Chi-square on matching
 - Concordance between surgical pairs with McNemar's test
 - Intra HIV+ cohort analysis by Fisher's Exact

Study was powered to detect a complication rate of $>5.7\%$ among HIV+ cases assuming complication rate among HIV- population is 1.5%

Results - 1

- Matching and exclusions from analysis

361 case / control pairs matched

66 pairs excluded from analysis

57 because 1/2 of pair chart not available

9 due to HIV/eligibility not confirmed in chart

295 pairs available for analysis

- Closeness of match among 295 analyzed pairs

Gender and procedure: exact match for all pairs

Age (yr of birth): 89% matched within 3 years

Year of surgery: 95% matched within 1 year

Medical center of surgery: 95% matched on facility

p value for all matches was > 0.1

Results - 2

- Surgical procedures among 295 pairs analyzed

| | |
|---------------------------------|-----|
| Hernia Repair (various forms) | 131 |
| Appendectomy | 54 |
| Cholecystectomy | 39 |
| Hip Replacement | 18 |
| Coronary Bypass | 15 |
| Mammoplasty | 9 |
| Bowel Resection/Rectal Surgery | 8 |
| Arthroscopy/Arthrotomy | 7 |
| Cardiac Valve Replacement | 4 |
| Knee Replacement (Total) | 4 |
| Laparoscopy/Laparotomy | 3 |
| Hysterectomy (+/- oophorectomy) | 3 |

Results - 3

| | <u>Cases</u> | <u>Controls</u> |
|--|--------------|-----------------|
|--|--------------|-----------------|

| | | |
|---------------|--------|--------|
| Gender (M/F): | 271/24 | 271/24 |
|---------------|--------|--------|

| | | |
|---------------|-----|-----|
| Percent male: | 92% | 92% |
|---------------|-----|-----|

| | | |
|-------------------|------|------|
| Median age (yrs): | 46.0 | 46.0 |
|-------------------|------|------|

| | | |
|-----------------|------|------|
| Mean age (yrs): | 46.8 | 46.9 |
|-----------------|------|------|

Mean difference in age (case/control): 0.23 years

| | | |
|-------------------|------|------|
| Hemoglobin (mean) | 13.5 | 14.0 |
|-------------------|------|------|

| | | |
|------------|-----|-----|
| WBC (mean) | 7.1 | 9.1 |
|------------|-----|-----|

- No significant difference with regards to ethnicity or comorbidities either.

Results - 4

- Characteristics of HIV+ cases at surgery (n=295)
 - Duration of known HIV infection: 8.4 years (median)
 - History of AIDS defining condition: 69%
 - History of opportunistic infection: 25%
 - CD4 mean (IQR*): 421 (237-557)
 - CD4 median: 380
 - CD4 < 200: 19%
 - CD4 > 500: 32%
 - HIV VL mean (IQR*): 19K (<500-4884)
 - HIV VL BLQ: 51.5%
 - HIV viral load < 500: 62%
 - HIV viral load > 10K: 19%

*IQR—Inter Quartile Range

Results - 5

| Measure | HIV+ Cases | HIV- Controls | <i>p</i> value |
|-------------------------|-----------------------|-----------------------|----------------|
| Known alive @ 12 months | 273/92.5% | 275/93.2% | >0.1 |
| Any complication | 36/12.2% | 29/9.8% | See next slide |
| >1 Complication | 5/1.7% | 2/0.7% | >0.1 |
| Wound infection | 13/4.4% | 13/4.4% | >0.1 |
| Revision surgery | 10/3.4% | 7/2.4% | >0.1 |
| LOS: median/ mean | 1.0 days/ 2.5 days | 1.0 days/ 2.3 days | >0.1 / >0.1 |
| Site infxn. @ 1 yr | 10/3.4% | 7/2.4% | >0.1 |
| Surgical fu visits | 1.0 visits | 1.0 visits | >0.1 |

Results - 6

| | | Surgical Complication in Control | |
|-------------------------------------|-----|-------------------------------------|-----|
| | | YES | NO |
| Surgical Complication in Case | YES | 6 | 30 |
| | NO | 23 | 236 |

Test of concordance between paired cases and controls with respect to presence of any post-op complication

$p=0.41$ (NS) McNemar's Exact

Results - 7

- Number of known deaths in 12 mo and cause

HIV+ Cases (n=9)

| | |
|-----------------|---|
| Lymphoma | 3 |
| Renal Failure* | 1 |
| Rectal CA | 1 |
| Resp. Failure | 1 |
| Non-surg sepsis | 1 |
| Gangrene* | 1 |
| Unknown | 1 |

HIV- Controls (n=2)

| | |
|------------|---|
| Hemorrhage | 1 |
| Rectal CA | 1 |

Paired Mortality (case/control): $p=.07$ by McNemar's Exact

*not related to surgery

Results - 8

CD4 and VL as predictors of complications among HIV+

| CD4 Level | Complications | | VL Level | Complications | |
|-----------|---------------|-----|----------|---------------|-----|
| | N | % | | N | % |
| <50 | 4/6 | 67% | <500 | 16/151 | 11% |
| 50-199 | 4/37 | 11% | 500-999 | 2/11 | 18% |
| 200-499 | 16/113 | 14% | 1K-9999 | 2/35 | 6% |
| 500+ | 8/78 | 10% | 10K-30K | 4/17 | 3% |
| | | | >30K | 8/22 | 36% |

CD4 < 200
vs.
CD4 ≥ 200

p=0.35

VL < 10,000
vs.
VL ≥ 10,000

p=0.008

Limitations of Study

- Potential surgical selection bias (e.g. perceived higher risk patients might not have gone to surgery)
- Chart review precluded blinding reviewer to patient's HIV status
- Surgical procedures outside of KPNC not captured (thought to be few)
- Lost to follow-up at 12 months for 13 cases (4%), 18 controls (6%)
- 66 pairs not yet available for analysis
- No CD4, VL before surgery for 9.2%, 9.8% respectively

Conclusions - 1

- This is the largest study of surgical outcomes in HIV+ adults reported to date.
- Surgical outcomes were similar between HIV+ cases and HIV- controls which were closely matched on age, gender, type of surgery, year and location of surgery.
- HIV+ status does not predict poorer surgical outcome. HIV status should not by itself be a criterion for surgical consideration.

Conclusions - 2

- Deaths among HIV+ patients in 12 months post-surgery were not likely due to surgical complication.
- A lower CD4 count does not increase risk of surgical complication.
- VL >10,000 may increase risk of surgical complication and bears additional study.

Coronary revascularization

- Boccara et al. P740
- French-Italian
- Prospective, case-control, matched for age and gender
- MACE: Major Adverse Cardiac Events: cardiac death, MI, repeat revascularization

Coronary Revasc. (2)

- **FRISCA 1**
- $n = 44$
- mean follow-up = 12 months
- CD4 mean 480
- No difference in MACE: including target lesion and target vessel revascularization

Coronary Revasc. 3

mean F/U 29 months

| • FRISCA 2 | <u>HIV +</u> | <u>HIV-</u> | |
|-------------------|--------------|-------------|---------|
| • n = | 19 | 38 | |
| • MACE | 11(58%) | 7(18%) | n=0.002 |
| • CV death | 0 | 0 | |
| • MI | 3(16) | 3(8) | n=.8 |
| • PCI | 5(26) | 4(11) | n=.12 |
| • reCABG | 3(16) | 0 | n=0.03 |

Coronary revascularization

- **Conclusions**
- Revascularization is feasible and safe
- Increase MACE in CABG, reasons unknown
- Larger prospective studies needed

Genotype vs Phenotype Resistance testing

- P134: Bertz et al. (including Havlir)
- 049 study
- Lopinavir Inhibitory Quotient (“IQ”) = [C-trough] / individual protein-adjusted IC50
- Randomized HIV-experienced patients to
 - LPV/r: 677/166 b.i.d. (n = 19)
 - LPV/r: 400/300 b.i.d. (n = 14)
 - both raise LPV trough by 60-70%

049 study, continued

- Median fold LPV IC50↑ 4.1 (0.6-273)
- Median IQ LPV = 27 (0.7-438)
- Median # active nRTI was 1 (0-3)
- Success: VL <400 wk 48 associated with
 - LPV IQ (p=0.03)
 - nRTI genotype (not phenotype; p=0.05)
 - baseline HIV RNA (p=0.03)

Genotype vs Phenotype test

- Blanco et al P675, Spain
- VIHRES comparing Antivirogram to G
- 166 patients; 158 randomized
- new regimen chosen by Virologist and Clinician
- Only predictor of success: >95% adherence
 - **OR: 3.8** G (p=0.036); **2.8** P (p=0.082)

VIHRES-2

| • | Geno | Pheno |
|-----------------|------|-------|
| • randomized | 78 | 58 |
| • compl 48 wks | 51 | 45 |
| • CD4+ baseline | 248 | 192 |
| • VL baseline | 4.6 | 4.52 |
| • Prev. HAART | 3.5 | 4.5 |

VIHRES-3

| | | Geno | Pheno |
|---|-------|-------|-------|
| • | VL | | |
| • | 12 wk | -1.44 | -1.42 |
| • | 24 wk | -1.78 | -1.62 |
| • | 36 wk | -1.8 | -1.55 |
| • | 48 wk | -1.7 | -1.6 |

VIHRES-4

| | | Geno | Pheno |
|---|-------|------|-------|
| • | CD4+ | | |
| • | 12 wk | +13 | +30 |
| • | 24 wk | +24 | +65 |
| • | 36 wk | +50 | +63 |
| • | 48 wk | +53 | +71 |

Role of 3TC in Rx failure

- Dragsted et al (P549): COLATE Trial
- Randomized 131 to 3 drugs +/- 3TC
- Primary objective: log₁₀ reduction in pVL following 48 wks Rx by Area Under Curve Changes from baseline (AAUCMB).
- Median baseline pVL 4.0, CD4+ 310, nadir CD4+ 125.

COLATE-2

- | | <u>+3TC</u> | <u>-3TC</u> |
|-------------|-------------|-------------|
| • 48 wks Rx | 54 (83%) | 60 (90%) |
| • AAUCMB | -1.4 | -1.5 |
| • <50/<400 | 52%/66% | 44%/65% |
- ALL COMPARISONS N.S.

LIPOATROPHY

- Noor et al (P722): Baseline TG levels predict development of lipoatrophy
- Summary of BMS 096 and 099
- Randomized, double-blind trials of stavudine 100 mg XR vs 40 mg b.i.d. IR.
- Lipoatrophy defined by investigator
- median F/U 116 wk (XR) and 114 wk (IR)

Risk of lipoatrophy

096/099-2

| | <u>OR</u> | <u>p</u> |
|----------------------|-----------|----------|
| • BL TG <200 vs >200 | .523 | 0.029 |
| • Age <40 vs >40 | .454 | 0.002 |
| • d4T IR vs XR | 1.975 | 0.003 |

Fragility Fractures

- McComsey et al P743
- 9 HIV clinics; 8600 patients
- 49 patients with fragility fractures following little or no trauma
- Outcome in 36, median F/U 10 months, recurrence 9 cases (18% of pts), 7 at new bone sites

Fragility fractures-2

- 10/49 patients with DEXA scans
- LS: median t-score -2.43 with 4/10 osteoporotic and 5/10 osteopenic
- Hip: median t-score -2.21, 4/10 each osteoporotic and osteopenic
- Any treatment offered 19/49 (39%)

Role of Alendronate

- Guaraldi et al P742, Italian
- n=41, on HAART, LS t-score <-1.0
- Randomized to A 70 mg q wk/Ca⁺⁺/Vit D vs Ca⁺⁺/Vit D alone
- Interim 52 week results

Alendronate-2

| • | Cases | Controls |
|--------------------|-------|----------|
| • # | 18 | 23 |
| • males | 72.2% | 69.6% |
| • CD4+ nadir | 184 | 141 |
| • #fx | 2 | 2 |
| • LS t-score | +4% | +3.7% |
| • Fem neck t-score | -0.5% | -3.4% |

Bone density in women

- Anastos and Hessel P744
- Women's Interagency HIV Study
- Compared bone density (DEXA) at 3 sites in n=
 - 88 HIV- any 6.4%
 - 90 HIV+ HAART- any 18.9%
 - 94 HIV+ HAART+ any 20.4%

Bone density in women-2

| <u>Variable</u> | <u>adj OR</u> | <u>p</u> |
|--|---------------|----------|
| • White race | 2.57 | 0.0505 |
| • BMI (per kg/m ²) | 0.89 | 0.0014 |
| • HIV infection | 3.14 | 0.0273 |
| • postmenopausal | 4.74 | 0.0005 |
| – longer NVP use associated with higher DEXA | | |
| – longer ABV use associated with lower DEXA | | |

Anal Cancer

- Poster discussion chaired by Joel Palefsky
- Highlighted importance of digital examination for diagnosis of cancer
- Benefit of CYTO-TEK liquid cytology over traditional swab/slide methodology
- CIS should be excised, not irradiated

Anal Cancer-2

- C. Mathews P775, Owen Clinic, UCSD
- Single examiner, using HRA
- 38 months, 2918 anal PAPs, 642 pts. with repeat at median 387 days, 154 with simultaneous PAP and colposcopic bx
- 1 invasive cancer identified (hx previous)
- Concordance of PAPs decreases as interval between tests increases

Anal cancer-3

- Sullivan et al P777; CDC
- 58,039 HIV+ persons; 231,450 PY, 150 with anorectal cancer between 1990-2002.
- Included diagnoses of HSIL/CIS
- Compared with SEER data base.

Anal Cancer-4

- Rate/100,000 PY
- HIV+, age/sex adj. 66.1
- general population 21.8
- Immunologic AIDS 80
- Clinical AIDS 110

Anal Cancer-5

- Adjusted OR for risk in persons HIV+
- MSM **5.6**
- Age, yrs >45 **2.5** vs 35-45 **1.7**
- Clinical AIDS **1.5**
- CD4+ <200 **4.0** vs 200-499 **2.4**

Anal Cancer-6

- Diamond et al P778
- San Diego County Registry 1988-2000
- Includes HSIL and CIS
- 39 cases, all men, 97% MSM, med CD4 120 (2-551), median age 42 years
- Rate 24.7/1000 cases AIDS in 2000
- 19 deaths, 6 (32%) of Anal cancer

Diagnosis of PCP

- Huang et al P768, SFGH
- mitochondrial RNA-based RT-PCR assay
- Oral wash: 10 cc N.S. gargled for <60s
- Distinguishes viable from non-viable PC
- 41 pts, 44 episodes of “R/O PCP”
- Sensitivity 69%; Specificity 94%

Epidemiology of PCP

- Zucchi et al P769 SFGH
- 1-5 OPW on same 41 patients, 18 w/o PCP
- | | Colonized | Non-colon. |
|--------------|-----------|------------|
| • N = | 13 | 5 |
| • CD4+ med. | 83 9-702 | 203 15-234 |
| • Hx PCP | 5 | 0 |
| • PCP proph. | 4 | 1 |