Update on EARLY GI-cancer

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E.Herriot Hospital
Lyon, France
Rationale
Epidemiology
Diagnosis
Treatment
Rationale

Epidemiology

Diagnosis

Treatment
Why do we need, as GI endoscopists, to be concerned by early GI cancer?

1- Health care improvement

2- Strategy
Health care improvement:

A carcinoma detected at early stage means better prognosis for the patient less cost for the society

* It does mean that we need to screen the whole population
Strategy for GI endoscopists:

Concerning advanced carcinomas,

- there is a increasing impact of chemotherapy (and radiotherapy) and less room for endoscopic palliation

Exemples: eso SCC, colonic cancer

- there is an increasing impact of radiology for the diagnosis

Exemple: MRCP replaced ERCP
Strategy for GI endoscopists:

Concerning advanced carcinomas,

There is a « competition » between oncologists and gastroenterologists for the management of cases and for fundings.

Gastroenterologists and endoscopists must focus on early GI-cancer and claim that the management of early GI-cancer is part of oncology and the future of GI oncology.
Rationale

Epidemiology

Diagnosis

Treatment
Are we effective, as GI endoscopists, to find early GI cancer?

Exemple: gastric carcinoma
### Ratio T1/ total gastric carcinomas

<table>
<thead>
<tr>
<th>Region</th>
<th>Ratio</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>40%</td>
<td>Osaka Cancer Registry 98</td>
</tr>
<tr>
<td>France</td>
<td>7%</td>
<td>Registre bourguignon 02</td>
</tr>
</tbody>
</table>

### 5y survival

<table>
<thead>
<tr>
<th>Region</th>
<th>Ratio</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>47%</td>
<td>Osaka Cancer Registry 98</td>
</tr>
<tr>
<td>Europe</td>
<td>22%</td>
<td>IARC 99</td>
</tr>
<tr>
<td>USA</td>
<td>19%</td>
<td>Bethesda 98</td>
</tr>
</tbody>
</table>
Japan

5 y survival

1975-77  26%
1987-89  45%
Why are we late in Occident?

1- Difference in incidence
2- Decreasing incidence
3- No limited high risk population
4- No symptoms
5- Low rate of polypoid lesions
6- Difference in endoscopic practice
1- Difference in incidence: number/year

<table>
<thead>
<tr>
<th></th>
<th>car colon</th>
<th>car gastric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan</td>
<td>48 000</td>
<td>115 000</td>
</tr>
<tr>
<td>Europe</td>
<td>186 000</td>
<td>77 000</td>
</tr>
</tbody>
</table>

2- Decreasing incidence 1963 → 1989

Japan: less 36%, Europe: less 43%

Globocan
France

60 millions inhabitants, 30 millions > 40y
1 million upper GI endosc / y
6000 new gastric car / y

We have to find 200 new asymptomatic cases/y

We are 2000 gastroenterologists

Each of us does 500 upper GI endoscopy
Each of us has to find one superficial gastric car / 10 years or one per 5000 patients
So 2.5 during our carreer
3- Low role of etiological factors

Atrophic gastritis: 1.8-2.5 (Inoue IJC 90 Sipponen EJ GH 94)
Intestinal metaplasia, *Helicobacter pylori*
Gastrectomy, Biermer
Familial types ++++++

Except rare familial types, no high risk population to be screened

4- No specific symptom or no symptom
5- Low ratio of polypoid lesions

3223 lésions stade 0 (class. Vienne-J SGE)
J Gastroenterol Mass Survey 2002

0-I  6%
0-II a  17%
0-II b  17%
Adenoma = 10% of gastric neoplasms
0-II c  70%
0-III  7%
0-IIc, sm 1 (M. Sasako)
6- Difference in endoscopic practice

Japan: standard gastric endoscopy

Exploration and picture zone by zone
Without (color abnormalities)
then with chromoscopy (pattern abnormalities)
Zoom if abnormality
Minimum: 10 minutes

Sensitivity for dg of superf. neoplasm: 81%
Hoskova Endoscopy 98
6- Difference in endoscopic practice

France: standard gastric endoscopy

Mean duration of gastric exploration: 130 sec

Sensitivity for diag of superficial neoplasms ??
Certainly <= 80%
Japanese endoscopists are better educated and more motivated to find flat lesions than European who are mainly looking for polypoid lesions.

Is it also true for colonic cancers or esophageal cancers?
# Esophageal carcinomas

<table>
<thead>
<tr>
<th>Source</th>
<th>T1/total</th>
<th>Tmuq/total</th>
</tr>
</thead>
<tbody>
<tr>
<td>J Nat Ca Center</td>
<td>42%</td>
<td>18%</td>
</tr>
<tr>
<td>Japanese enquiries</td>
<td>25%</td>
<td>6%</td>
</tr>
<tr>
<td>Burgundy enquiry</td>
<td>4%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

Despite prevalence of esophagus cancer, Burgundy > Japan
KUDO S 2003

10357 superficial lesions: adenomas or adenocarcinomas

Adenocar & severe dysplasia: 961 (9.3%)
<table>
<thead>
<tr>
<th>Diameter</th>
<th>Polypoïds (57%)</th>
<th>Flats (41%)</th>
<th>Depressed (2.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5 mm</td>
<td>0%</td>
<td>0.1%</td>
<td>8.1%</td>
</tr>
<tr>
<td>6-10</td>
<td>1.3%</td>
<td>0.6%</td>
<td>29.2%</td>
</tr>
<tr>
<td>11-15</td>
<td>9.4%</td>
<td>1.1%</td>
<td>68.8%</td>
</tr>
<tr>
<td>16-20</td>
<td>17.4%</td>
<td>9.8%</td>
<td>83.3%</td>
</tr>
<tr>
<td>&gt;20 mm</td>
<td>30.7%</td>
<td>23%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Depressed lesions = « cancer de novo »
Earla carcinoma

Ca II a

Ca II c
Japanese endoscopist experience in Europe

Watanabe, Stockholm

232 pts with superficial neoplasms

<table>
<thead>
<tr>
<th>Type</th>
<th>Kc</th>
<th>Kc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flat lesions</td>
<td>95 (41%)</td>
<td>9 (10%)</td>
</tr>
<tr>
<td>Depressed lesions</td>
<td>14 (6%)</td>
<td>6 (43%)</td>
</tr>
</tbody>
</table>
Fujii, Leeds
722 consecutive pts, 166 superf neo.

<table>
<thead>
<tr>
<th>Car</th>
<th>Polypoïds</th>
<th>Flats</th>
<th>Depressed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 (60%)</td>
<td>61 (6%)</td>
<td>5 (3%)</td>
</tr>
<tr>
<td></td>
<td>9 (19%)</td>
<td>7 (11%)</td>
<td>4 (80%)</td>
</tr>
</tbody>
</table>

« If we miss
- the flat adenomas, we miss 35% of car
- the depressed lesions, we miss 20% of car »
Saitoh 99
Japanese observer in an endoscopy unit in Texas

Number of neoplastic lesions: + 125%

Teixeira 2000
Brasilian endoscopist, education in Japan

13 depressed lesions found on 3.5y = 1 for 100 pts
Why Japanese endosc see more lesions than European endosc?

Education of vision:
- Small abnormalities of relief
- Small abnormalities of colour +++:
  - erythroplastic (flat, depressed)
  - or whitish (elevated)
- Less lumen inflation
- Analysis during peristaltic wave
- More accurate analysis of the pattern
- Motivation to find small lesions
Rationale

Epidemiology

Diagnosis

Treatment
Diagnosis: How to improve?

MUCOSA (Patient)

OPERATOR

ENDOSCOPE
Diagnosis: How to improve?

MUCOSA (Patient)

OPERATOR

ENDOSCOPE
How to improve ? MUCOSA

1- to select mucosa at risk

= Screening

2- to make analysis of the mucosa easier
Mass screening of colorectal carcinoma
exemple: Hemoccult II, if positive colonoscopy (mortality/cancer decreases)

2002

2007: National
Ille-et-Vilaine

Number of tests: 90877

Compliance to test: 54%

Compliance to colonoscopy if test positive: 82%

Number of detected cancers: 207 (61% T1)
Esophageal squamous cell carcinoma

Systematic lugol staining in high risk pts French study (SFED)
1098 pts, 45 centers, systematic Lugol

RATE

History of ENT cancer: 393 pts 6.8% 37% T1
Chronic pancreatitis: 76 pts 0%
Alcoholic cirrhosis: 220 pts 3.2%
Alcohol-tobacco abuse: 408 pts 2.4%
How to improve MUCOSA?

1- to select mucosa at risk

= Screening

Only screening of colonic carcinoma and of esophageal SC carcinoma in ENT patients could be cost effective and should be organized
How to improve MUCOSA?

1- to select mucosa at risk
   = Screening

2- to make analysis of the mucosa easier
   = To improve patient tolerance
To improve patient tolerance =
- to organize sedation
- but also to reduce the need for sedation
  in order to reduce cost and constraints

transnasal endoscopy $\rightarrow$ upper GI

capsule $\rightarrow$ new colonoscopes $\rightarrow$ lower GI
If we also suppress the need for endoscope reprocessing ..... 
and colonic prep.......
Example 1: nasogastroscopy

Video 5 mm
one plan bending

Single-use sheath
Vision sciences
65 cm
operating channel
diameter: 5.1mm
500 pts, 10 centers, randomized study oral standard vs naso

- Sensation asphyxia: P < 0.0001
- Retching: P < 0.0001
- Discomfort: P < 0.0001
- Bloating: P < 0.001
- Gagging: P < 0.0001
- SCORE: P < 0.0001
Number of pts refusing another procedure in the same conditions:

Oral gastroscopy: 25.2%  
Nasogastroscopy: 10.3%  

p<0.001
Nasogastroscopy is very popular and considered to be very helpful in France
First procedure in Lyon, E.Herriot Hospital
Then rapid expansion to Rhône-Alpes region and then to France

In Lyon,
83% of upper GI diagnostic endoscopies
6 nasogastroscopes in E.Herriot Hospital
3 nasogastroscopes in a large private hospital

In France,
139 nasogastroscopes sold in 2004
Exemple 2: Esophageal videocapsule

Eliakim endosc06
« pillcam »
Esophageal Capsule
Eliakim

Still under evaluation
Example 3

Self-propelling single-use colonoscope

- Aer-O-scope
- Invendo
- Colonosight
- Cathcam
- ..............

Still under evaluation
SOME EXEMPLES ....

2 technologies

1- single use sheath
2- pneumatic advance
Still under evaluation
CathCam Guide Wire-Directed Colonoscopy: First Pilot Study in Patients with a Previous Incomplete Colonoscopy

A. Fritscher-Ravens¹
S. Fox²
C. P. Swain¹
P. Milla³
G. Long⁴

Still under evaluation
Diagnosis: How to improve?

MUCOSA (Patient)

OPERATOR

ENDOSCOPE
CHROMOSCOPY
HIGH DEFINITION VIDEO
STRUCTURE ENHANCEMENT
MAGNIFICATION
NARROW BAND IMAGING: IHb color enhancement
FLUORESCENCE INTERFEROLOGY
CONFOCAL MICROSCOPY: 1 microm
ENDOCYSTOSCOPY
ELASTIC SCATTERING: subcell
RAMAN SPECTROSCOPY: molecule
DIAGNOSIS = 3 steps

I try to detect one lesion

There is a lesion

What is it?

It is a neoplasm

Which is its extension?

Detection → Characterization → Staging
The main target = improvement in detection

Why?

first step, need ++++: no alternative

caracterisation = biopsy
« optic biopsy » is a secondary target
staging = EUS, .... surgery
Improvement in detection

Dysplasia

High grade dysplasia
Which are the best candidates?
CHROMOSCOPY
HIGH DEFINITION VIDEO
STRUCTURE ENHANCEMENT
MAGNIFICATION
NARROW BAND IMAGING, IHb color enhancement
FLUORESCENCE
INTERFEROMETRY: 10 microm
CONFOCAL MICROSCOPY: 1 microm
ENDOCYSTOSCOPY
ELASTIC SCATTERING: subcell
RAMAN SPECTROSCOPY: molec
Spectrum

Conventional

NBI
CHROMOSCOPY
HIGH DEFINITION VIDEO
STRUCTURE ENHANCEMENT
MAGNIFICATION
NARROW BAND IMAGING, IHb color enhancement

FLUORESCENCE
INTERFEROMETRY: 10 microm

CONFOCAL MICROSCOPY: 1 microm
ENDOCYSTOSCOPY
ELASTIC SCATTERING: subcell

RAMAN SPECTROSCOPY: molec
Autofluorescence
Olympus AFI Colon

Juntendo University
Autofluorescence
Olympus AFI Barrett
Kara GIE 05
CHROMOSCOPY
HIGH DEFINITION VIDEO
STRUCTURE ENHANCEMENT
MAGNIFICATION
NARROW BAND IMAGING, IHb color enhancement
FLUORESCENCE
INTERFEROMETRY: 10 microm
CONFOCAL MICROSCOPY: 1 microm
ENDOCYSTOSCOPY
ELASTIC SCATTERING:
RAMAN SPECTROSCOPY: molec

Too punctual
DIAGNOSIS = 3 steps

I try to detect one lesion

Detection

There is a lesion

Characterization

What is it?

Staging

It is a neoplasm

Which is its extension?
CHROMOSCOPY
HIGH DEFINITION VIDEO
STRUCTURE ENHANCEMENT
MAGNIFICATION
NARROW BAND IMAGING, FLUORESCENCE
INTERFEROMETRY
CONFOCAL MICROSCOPY
ENDOCYSTOSCOPY
ELASTIC SCATTERING
RAMAN SPECTROSCOPY

Detection
Characterization
Adenoma

Kiesslich
Colonic cancer

Kiesslich
Finally…….
Rationale
Epidemiology
Diagnosis
Treatment
Treatment of early GI cancer

We have to manage the risk of recurrence, of metachronous lesion, of lymph node, ...

We need to apply the same principles as used in surgery
Treatment of early GI cancer

First principle
RESECTION >>> TUMOR DESTRUCTION (PDT, APC, ....)

Specimen for histopathology
ANALYZIS of the SPECIMEN

STRETCHING ON A BOARD WITH PINS

1- Complete resection ?
laterally and in depth
2- Invasiveness of carcinoma ?

TO RECONSIDER SURGERY
main advantage on methods based on tumor destruction
One exception to this rule? BARRx

Generator of radiofrequency

Electrodes
Swine, Ganz, 10 J/cm²

Prior tt

After tt
32 pts: Barrett, no dysplasia
1 sec ablation, 10 J/cm²
no residual intestinal metaplasia (357 biopsies)
no stenosis
Second principle

Complete resection
One piece
Security margin
Complete resection, security margin
In situ car

Invasive car

Piece-meal to be avoided
Mucosal resection
+/- piece meal

Mucosal dissection
IT knife
Needle knife
Flex knife
Hook knife
Third principle

To treat our complications
Coag >> clips
NB:
In case of perforation, even following clipping we still need surgical advice and F-U with surgeons.....
Fourth principle

To prevent metachronous lesion = to treat the mucosa at risk
Circumferential esophageal muc. resection

Lyon, E. Herriot hospital: 32 cases, mean F-U: 19 mo
12 stenoses

Giovannini endosc 04: 21 cases, mean F-U: 18 mo
3 recurrences
9% bleeding, no stenosis

Soehendra Endosc 04: 12 cases, median F-U: 9 mo
no recurrence
2 stenoses
Fifth principle

To know the limits of endoscopy

= to evaluate the risk of lymph node metastases
EUS is not enough effective to detect metastatic lymph node

N status is dependent of T status

Evaluation of N status related to T status has been conducted by Japanese authors on surgical specimen

Definition of frontiers based on T status
Well differentiated
No vasc or lymph invasion
How to assess submucosal invasion?
II a + II c

II c + II a

II a + II c
EUS miniprobe 20-30 MHz

Musc. mucosae

9 layers
Case 4

1800 μm
CONCLUSIONS

1- Health care and strategy
2- Japan > Occident
3- Dg: not only a question of technology but of motivation and organization (screening)
4- Technology concerns images but also easiness (cost, compliance). To improve detection is the first target.
5- Treatment: same principles as surgery
Thank you